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UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

MEIJER, INC. and MEIJER DISTRIBUTION, INC., Plaintiffs, vs. WYETH, INC. and TEVA PHARMACEUTICALS USA, INC., Defendants.	CASE NO. COMPLAINT AND DEMAND FOR JURY TRIAL

TABLE OF CONTENTS

Page

Plaintiffs Meijer, Inc. and Meijer Distribution, Inc., bring this civil action against Defendants Wyeth, Inc. and Teva Pharmaceuticals USA, Inc. under the antitrust laws of the United States. Plaintiffs allege, based on personal knowledge as to themselves and on information and belief as to other allegations:

I. INTRODUCTION

1. This case is another in a string of pharmaceutical antitrust cases challenging anticompetitive conduct by brand and generic prescription drug manufacturers to delay generic entry and reap monopoly profits on the sales of their products during the period of delay.

2. This is an action challenging an unlawful and anticompetitive scheme by Defendant Wyeth, Inc. ("Wyeth") to maintain monopoly power and delay the entry of generic versions of Wyeth's Effexor XR, an encapsulated extended release version of the compound venlafaxine hydrochloride, including an independently unlawful agreement between Wyeth and Defendant Teva Pharmaceuticals USA, Inc. ("Teva"). Although Wyeth's marketing exclusivity for the original compound patent for Effexor XR lapsed on June 13, 2008, the first generic equivalent was foreclosed for two more years, until July 2010, and other generics (including Wyeth's authorized generic) remained foreclosed until June 2011. The reason: Wyeth engaged in an overarching anticompetitive scheme to prevent and delay the approval and marketing of generic versions of Effexor XR. Wyeth's scheme

included (i) fraudulently procuring three patents for extended release formulations of venlafaxine hydrochloride, (ii) wrongfully listing those patents in the FDA Orange Book; (iii) engaging in serial sham litigation to block and delay generic entry; (iv) entering into a horizontal market-allocation and price-fixing agreement with Teva to delay the entry of generic Effexor XR by Teva, Wyeth, and other generic manufacturers; and (v) negotiating settlements with subsequent generic applicants to preserve and protect its monopoly and the market-division agreement negotiated with Teva.

3. Wyeth obtained three method of use patents: the '171 patent, the '958 patent, and the '120 patent. These three patents ostensibly extended Wyeth's monopoly on extended release venlafaxine hydrochloride by nine years, until March 20, 2017. But Wyeth was only able to obtain these patents by misrepresenting material information to the Patent and Trademark Office (PTO). Under the stark light of patent infringement litigation, Wyeth knew there was no realistic likelihood that a court would enforce the '171, '958, or '120 patents against a generic manufacturer.

4. *The Nausea Fraud.* Wyeth obtained method of use claims for extended release venlafaxine by fraudulently claiming clinical data showed that Wyeth's extended release version of venlafaxine hydrochloride, Effexor XR,

reduced the incidence of nausea and vomiting associated with instant release Effexor.

5. *The Unexpected Discovery Fraud*. Wyeth fraudulently claimed that its purported discovery of an extended release version of Effexor was unexpected, despite knowing (i) an earlier Wyeth patent (the Upton patent) and a patent application by a Wyeth collaborator (the '589 PCT application) previously disclosed extended release versions of Effexor and (ii) one skilled in the art would be aware of several methods for achieving extended or sustained release formulations.

6. *The Prior Rejection Fraud.* Wyeth obtained method of use claims for extended release venlafaxine by failing to disclose that its own Upton patent disclosed extended release venlafaxine. Wyeth further failed to disclose that the original patent examiner had found its method of use claims unpatentable in light of the Upton patent, and that Wyeth had agreed with this rejection.

7. *The Inderal Fraud*. Wyeth fraudulently claimed that it was "completely unexpected" that an extended release venlafaxine hydrochloride formulation could be obtained because the hydrochloride of venlafaxine was extremely water soluble despite having developed the Effexor XR formulation by substituting venlafaxine for propranolol in the extended release formulation for its pre-existing Inderal LA product. Contrary to the representation to the PTO, Wyeth

expected this formulation to work because venlafaxine and propranolol have similar solubilities in water and peak blood levels that occur in about six hours. Wyeth failed to disclose the method by which it developed Effexor XR using the Inderal LA formulation or the Inderal LA label which contradicted its arguments to the PTO that extended release propranolol was irrelevant to extended release venlafaxine.

8. Wyeth used the fraudulently obtained patents to block generic versions of Effexor XR from the market by listing these patents in the Orange Book and promptly filing baseless patent infringement litigation against each and every generic manufacturer that tried to bring a generic extended release venlafaxine product to market, thereby triggering the automatic two-and-a-half year stays of FDA approval provided by the Hatch Waxman amendments. Wyeth asserted that generic manufacturers were infringing its method of use patents – patents Wyeth knew to be invalid and/or unenforceable – in seventeen sham lawsuits. The generic manufacturers uniformly responded by pointing out that Wyeth's method of use patents were invalid and/or unenforceable.

9. Wyeth listed the patents and initiated the sham infringement suits against Teva, the first generic company to seek to sell generic Effexor XR, and 16 subsequent generic manufacturers, despite knowing that the method of use patents were fraudulently obtained, invalid, and/or unenforceable. Without the invalid

and/or unenforceable patents, Wyeth could not have manipulated the Hatch-Waxman statute to exclude generic versions of Effexor XR. Generic manufacturers would have obtained FDA approval to sell their much less expensive extended release venlafaxine products at least two years earlier.

10. Wyeth settled each and every lawsuit before a court determined whether the '171, '958, and '120 patents were invalid and/or unenforceable. The settlements prolonged Wyeth's market exclusivity far beyond its lawful expiration in mid-2008, and enabled Teva to maintain and extend its generic exclusivity rights, while also providing Teva with significant additional benefits in exchange for its agreement not to market its generic version of Effexor XR until June 2010. Those benefits included reciprocal agreements by Wyeth not to compete with Teva during its period of generic exclusivity by launching an authorized generic version of the drug and to seek to preserve Teva's exclusivity by resolving any subsequent generic lawsuits before they advanced to findings of invalidity and/or non-infringement that would have triggered Teva's exclusivity.

11. If Wyeth had not fraudulently obtained the method of use patents, had not listed those patents in the Orange Book, had not brought sham infringement actions, and/or had not colluded with Teva to delay generic entry, generic extended release products would have launched for sale in June of 2008. Absent the fraud and other wrongful conduct alleged below, Wyeth could not have extended its

monopoly in the market for extended release venlafaxine hydrochloride capsules beyond June 2008.

12. As a result of Defendants' exclusionary conduct, generic versions of Effexor XR were illegally blocked from the marketplace from June 2008 through at least June 2010. During this period of foreclosure, U.S. annual sales of Effexor XR topped $2.5 billion. Direct purchasers paid significantly more for extended release venlafaxine hydrochloride capsules during this two year window (and continue to pay more for Effexor XR and its generic equivalents) than they would have paid in the absence of Defendants' illegal and anticompetitive acts.

II. JURISDICTION AND VENUE

13. This action arises under sections 1 and 2 of the Sherman Act, 15 U.S.C. §§ 1 & 2, and section 4 of the Clayton Act, 15 U.S.C. §15(a), to recover treble damages and other relief for the injuries sustained by Plaintiffs as a result of Defendants' unlawful foreclosure of the market for extended release venlafaxine hydrochloride capsules. The Court has subject matter jurisdiction under 28 U.S.C. §§ 1331 and 1337(a).

14. Wyeth and Teva transact business within this district. Venue is appropriate within this district under section 12 of the Clayton Act, 15 U.S.C. § 22, and 28 U.S.C. §1391(b) and (c).

III. THE PARTIES

15. Plaintiffs Meijer, Inc. and Meijer Distribution, Inc. (collectively, "Meijer" or "Plaintiffs") are corporations organized under the laws of the State of Michigan, with their principal place of business located at 2929 Walker Avenue, NW, Grand Rapids, Michigan 49544. Meijer is the assignee of the claims of certain direct purchasers which, during the relevant period, purchased Effexor XL directly from Wyeth (and resold at least some of it to Meijer) and suffered antitrust injury as a result of Defendants' anticompetitive conduct alleged herein.

16. Defendant Wyeth, Inc. is a Delaware corporation having its principal place of business at Five Giralda Farms, Madison, New Jersey 07940. Before 2002, Wyeth was known as American Home Products Corporation. Since October 2009, Wyeth has been a wholly owned subsidiary of Pfizer, Inc. Wyeth is in the business of developing, manufacturing and marketing brand-name pharmaceutical products.

17. Defendant Teva Pharmaceuticals USA, Inc. is a Delaware corporation having its principal place of business at 1090 Horsham Road, North Wales, Pennsylvania 19454. Teva is in the business of developing, manufacturing and marketing pharmaceutical products, primarily generic products, in the United States.

18. Throughout this complaint, the phrase "the Wyeth applicants" refers to Wyeth, the named inventors of the '171, '958, and '120 patents, the prosecuting attorneys of the '171, '958, and '120 patents, and agents thereof. The Wyeth applicants include, but are not limited to: inventors John C. Clark, John U. Lamer, Deborah M. Sherman, and Steven A. White as well as attorneys Ronald W. Alice, Rebecca Barrett, Egon Berg, Robert Boswell Jr., Steven R. Eck, and Arthur Seifert. The term also includes any agents from Wyeth of these persons.

IV. LEGAL BACKGROUND

A. The Regulatory Structure for Approval of Generic Drugs and Substitution of Generics for Brand Name Drugs

19. Under the Federal Food, Drug, and Cosmetic Act ("FDCA"), manufacturers who create a new drug product must obtain the approval of the FDA to sell the new drug by filing a New Drug Application ("NDA"). 21 U.S.C. §§ 301-392. An NDA must include submission of specific data concerning the safety and effectiveness of the drug, as well as any information on applicable patents. 21 U.S.C. § 355(a), (b).

20. When the FDA approves a brand name manufacturer's NDA, the brand manufacturer may list any patents that the brand manufacturer believes could reasonably be asserted against a generic manufacturer who makes, uses, or sells a generic version of the brand name drug prior to the expiration of the listed patents in the FDA's book of Approved Drug Products with Therapeutic Equivalence

Evaluations, commonly referred to as the "Orange Book." Patents issued after NDA approval may be listed within 30 days of issuance. 21 U.S.C. §§ 355 (b)(1) & (c)(2).

21. The FDA relies completely on the brand name manufacturer's truthfulness about patents' validity and applicability; the FDA has neither the authority nor the resources to check the manufacturer's representations for accuracy or trustworthiness.

1. The Hatch-Waxman Amendments

22. The Hatch-Waxman Amendments enacted in 1984 simplified the regulatory hurdles for prospective generic manufacturers by eliminating the need for them to file lengthy and costly NDAs. *See* Drug Price Competition and Patent Term Restoration Act, Pub. L. No. 98-417, 98 Stat. 1585 (1984). A generic manufacturer seeking approval to sell a generic version of a brand name drug may now file an abbreviated new drug application (ANDA). ANDAs rely on the scientific findings of safety and effectiveness included in the brand name drug manufacturer's original NDA, but must show that the generic drug contains the same active ingredient(s), dosage form, route of administration, and strength as the brand name drug – that is, that the generic drug is bioequivalent to the brand name

drug. The FDA assigns generic drugs that are bioequivalent to branded drugs an "AB" rating.[1]

23. The FDCA and Hatch-Waxman Amendments operate on the presumption that bioequivalent drug products containing identical amounts of the same active ingredients in the same route of administration and dosage form, and meeting applicable standards of strength, quality, purity and identity, are therapeutically equivalent and may be substituted for one another. Thus, bioequivalence demonstrates that the active ingredient of the proposed generic drug would be present in the blood of a patient to the same extent and for the same amount of time as the branded counterpart. 21 U.S.C. § 355(j)(8)(B).

24. Throughout the Hatch-Waxman Amendments, Congress sought to expedite the entry of legitimate (non-patent infringing) generic competitors, thereby reducing healthcare expenses nationwide. Congress also wanted to protect pharmaceutical companies' incentives to create new and innovative products.

[1] Generic manufacturers can also seek approval of non-AB-rated generics. The FDCA permits "hybrid" applications that are neither full NDAs containing safety and efficacy data, nor ANDA applications showing that the proposed product is the "same" as the NDA product. 21 U.S.C. § 505(b)(2). Drug products approved under this section use a safe and effective active pharmaceutical ingredient, but modify the drug product in some way so that it differs from the original NDA product, either in dosage form, strength, route of administration, formulation, dosing regimen, or indication. These non-AB-rated generics are not bioequivalent to the innovator product. See 21 CFR 314.54.

25. The Hatch-Waxman Amendments achieved both goals, substantially advancing the rate of generic product launches, and ushering in an era of historic high profit margins for brand name pharmaceutical companies. In 1983, pre-Hatch Waxman Amendments, only 35% of the top-selling drugs with expired patents had generic versions available; by 1998, nearly all did. In 1984, prescription drug revenue for branded and generics totaled $21.6 billion and generic drugs accounted for 18.6% of prescriptions. By 2009, total prescription drug revenue had soared to $300 billion and generic drugs accounted for 75% of prescriptions.

2. Paragraph IV Certifications

26. To obtain FDA approval of an ANDA, a generic manufacturer must certify that the generic drug addressed in its ANDA will not infringe any patents listed in the Orange Book. Under Hatch-Waxman, a generic manufacturer's ANDA must contain one of four certifications:

i. that no patent for the brand name drug has been filed with the FDA (a "Paragraph I certification");

ii. that the patent for the brand name drug has expired (a "Paragraph II certification");

iii. that the patent for the brand name drug will expire on a particular date and the generic company does not seek to market its generic product before that date (a "Paragraph III certification"); or

iv. that the patent for the brand name drug is invalid or will not be infringed by the generic manufacturer's proposed product (a "Paragraph IV certification").

27. If a generic manufacturer files a Paragraph IV certification, a brand name manufacturer has the ability to delay FDA approval of an ANDA simply by suing the ANDA applicant for patent infringement. If the brand name manufacturer initiates a patent infringement action against the generic filer within 45 days of receiving notification of the Paragraph IV certification, the FDA may not grant final approval to the ANDA until the earlier of (a) the passage of 30 months, or (b) the issuance of a decision by a court that the patent is invalid or not infringed by the generic manufacturer's ANDA. The FDA may grant "tentative approval," but cannot authorize the generic manufacturer to go to market.

28. As an incentive to spur generic companies to seek approval of generic alternatives to branded drugs, the first generic manufacturer to file an ANDA containing a Paragraph IV certification gets a period of protection from competition with other generic versions of the drug. For Paragraph IV certifications made prior to December 2003, the first generic applicant is entitled to 180 days of market exclusivity. Meaning, the first approved generic is the only available generic for at least six months.

29. The ability of brand name manufacturers to delay FDA approval of an ANDA for up to 30 months merely by filing suit upon receipt of notice of a paragraph IV certification is a strong incentive to brand name manufacturers to list patents in the Orange Book – even if such patents are not eligible for listing – and

sue any generic competitor that files an ANDA with Paragraph IV certifications – even if the competitor's product would not actually infringe the listed patent(s).

B. The Benefits of Generic Drugs

30. Typically, AB-rated generics cost much less than their branded counterparts. Over time, as more generic equivalents compete with each other, prices decline even further. Since passage of the Hatch-Waxman Amendments, every state has adopted substitution laws that either require or permit pharmacies like those operated by Plaintiffs to substitute AB-rated generic equivalents for branded prescriptions unless the prescribing physician has specifically ordered otherwise.

31. Once a generic equivalent hits the market, the generic quickly overtakes sales of the branded drug. More than 90 percent of prescriptions for drugs that are available in both branded and generic forms are filled with a generic. The speed with which generic drugs take over the market appears to be increasing: in a sample of drugs losing patent protection between 1991 and 1993, generics on average held a 44 percent market share after one year; by 2008, generic versions could capture as much as 86 to 97 percent of the market within the first month.

32. Branded manufacturers are well aware of generics' steady erosion of their previously monopolized market. Branded manufacturers thus seek to extend

their monopoly for as long as possible, sometimes resorting to any (illegal) means possible.

V. OPERATIVE FACTS

A. Wyeth Obtains the Original Compound Patent for Effexor

33. On August 13, 1985, the U.S. Patent and Trademark Office (PTO) issued a patent for the compound venlafaxine hydrochloride ("venlafaxine"), U.S. Patent No. 4,535,186 (the Husbands patent). The inventors G.E. Morris Husbands, John P. Yardley, and Eric A. Muth assigned the Husbands patent to American Home Products Corporation – later Wyeth.

34. Eight years later, on December 28, 1993, the FDA approved Wyeth's ANDA for Effexor, an antidepressant whose active pharmaceutical ingredient is venlafaxine. Effexor is a tablet that dissolves rapidly, resulting in a rapid increase in blood plasma levels of venlafaxine shortly after administration. Compounds with such rapid dissolution profiles are referred to as "instant release" formulations. Levels of venlafaxine in the blood decrease over time, reaching subtherapeutic levels in about twelve hours. Effexor is thus usually taken twice a day.

35. The Husbands patent protected Wyeth's venlafaxine products by blocking generic equivalents from entering the market until June 13, 2008 (expiry of the patent would have occurred years earlier, but Wyeth received a significant

extension to reflect the NDA approval time period for Effexor, and an additional six month extension for having conducted pediatric studies). As a result, the Husbands patent provided Wyeth with 14 ½ years of market exclusivity for both instant release and extended release venlafaxine hydrochloride. This lawful period of market exclusivity allowed Wyeth to market its venlafaxine products – both Effexor and Effexor XR – without generic competition, resulting in huge sales and profits to Wyeth. But the *quid pro quo* of the patent system is that after those 14½ years, generic companies should have been in a position to launch competing products at markedly lower prices that benefit American purchasers.

B. Wyeth Schemes to Extend its Extended-Release Venlafaxine Monopoly

36. Although the original Husbands patent – and the PTO's extensions for NDA approval and pediatric studies – provided Wyeth with 14½ years of market exclusivity for venlafaxine products, this was not enough for Wyeth. Wyeth sought to extend the length of its exclusivity *even further*. Wyeth sought to obtain patents for the routine development of an extended release form of venlafaxine. Wyeth knew that it was working in an already crowded area of intellectual property art and that the extended release venlafaxine formulation was in no way a new invention. Yet it persisted, misrepresenting the prior art and its clinical tests, all in an effort to gain market exclusivity beyond its lawful 14½ years.

37. In the 1990's, methods for achieving sustained or extended release of the active ingredient in pharmaceuticals were well known in the industry. It was common knowledge that the rate of drug release from solid dosage forms could be extended by (a) modifying drug dissolution by controlling access of biologic fluids to the drug through use of barrier coatings, (b) controlling drug diffusion rates from dosage forms, and (c) chemical reaction or interaction between drug substance or its pharmaceutical barrier to site-specific biologic fluids. These methods use coated beads, granules, and microspheres; micro-encapsulated drugs; sustained-release, extended-release, timed-release, controlled-release, or continuous-release tablets or capsules; or embedding the drugs in slowly eroding or hydrophilic matrix systems.

38. Given the industry's knowledge and prior art, Wyeth knew it would be difficult, if not impossible, to legitimately obtain a patent for extended release formulations of venlafaxine. Even if a particular formulation could be patented, it would only prevent generics from designing around those formulation patents by developing non-infringing formulations of extended release venlafaxine.

39. Consequently, Wyeth adopted a "method of use" strategy, and set out to patent independent claims that broadly covered methods of using extended release venlafaxine, methods that were not tied to any specific formulation. Wyeth

knew that there must be something new, novel, or surprising about the methods of use in order to make its extended release venlafaxine patentable.

40. Even without patent protection beyond the original Husbands patent, Wyeth would have enjoyed more than ten years of market exclusivity for Effexor XR. But in the absence of any additional exclusivities, Effexor XR would have faced generic competition in June of 2008, the expiration date of the Husbands patent.

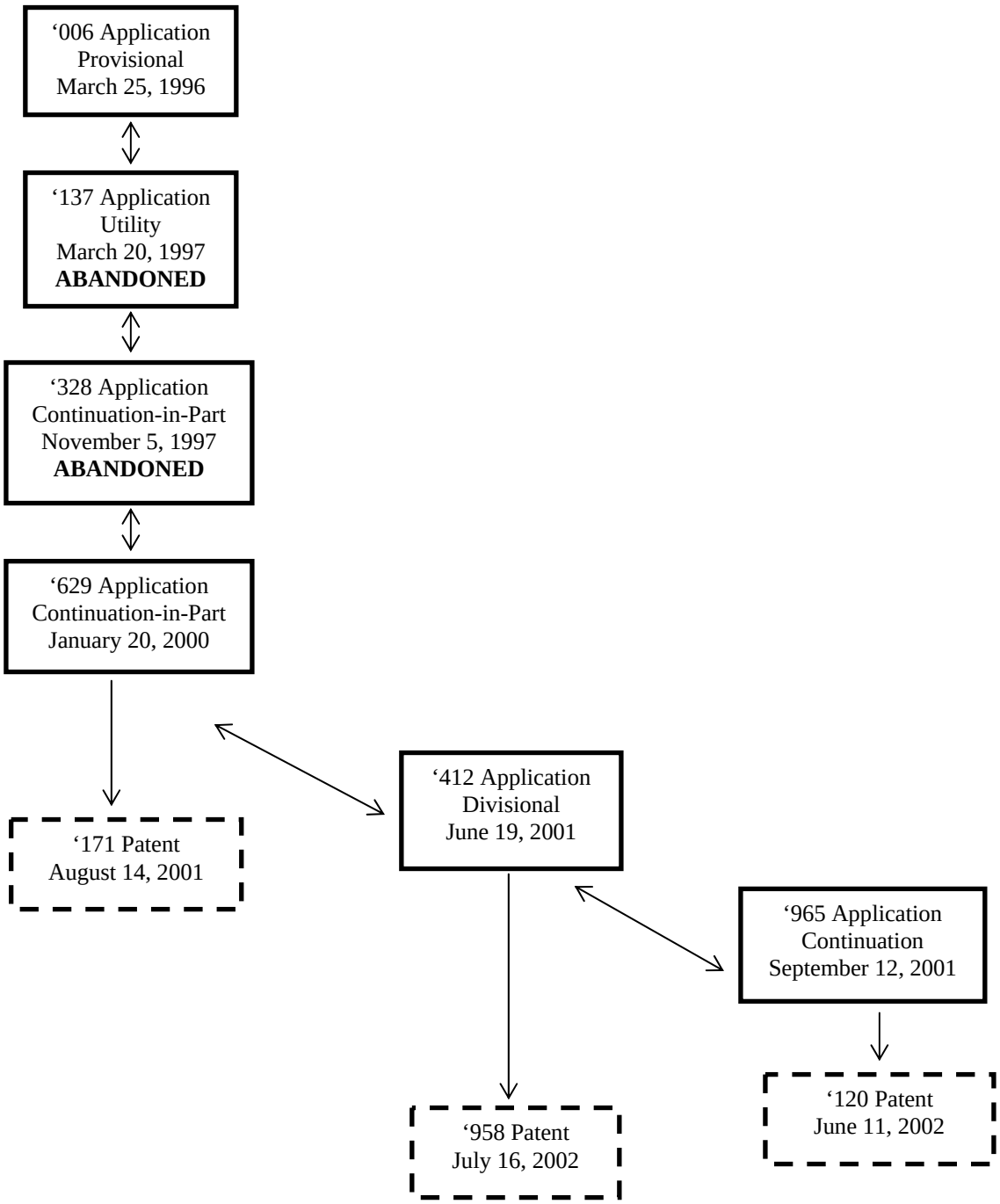
C. Wyeth Fraudulently Obtains Three Method of Use Patents for Effexor XR

41. On March 25, 1996, the Wyeth applicants filed an application that would eventually mature into a series of method of use patents for extended release venlafaxine hydrochloride. Two months later, on May 16, 1996, Wyeth sought FDA approval to sell an encapsulated extended release formulation of venlafaxine hydrochloride called Effexor XR. On October 20, 1997, the FDA approved Wyeth's NDA for Effexor XR. Effexor XR is typically taken once a day.

42. Wyeth submitted six sequential applications that led to three method of use patents, the '171, '958, and '120 patents. All three patents are, and have always been, unenforceable; they only issued because Wyeth defrauded the PTO. These patents prevented generics from coming to market in June of 2008.

43. A brief summary of Wyeth's patent application history follows. Wyeth's fraud in securing these patents is then described in detail.

1. The Application History of the Invalid and/or Unenforceable '171, '958, and '120 Patents



a. Wyeth's Original '006 Application

44. On March 25, 1996, the Wyeth applicants filed a provisional utility patent application, No. 60/014,006 (" '006 application") with the PTO. A utility patent application seeks to protect a new, useful, or nonobvious process or composition. Provisional patent applications require only a brief written description of the claimed subject matter. Inventors must file a non-provisional application with formal claims within one year. Filing a provisional application essentially allows an inventor to establish a date of invention one full year before the inventor actually submits evidence of his invention's patentability.

b. Wyeth's '137 Application

45. Almost exactly one year after filing the provisional application, on March 20, 1997, the Wyeth applicants filed a non-provisional application, No. 08/821,137 (" '137 application"). The '137 application claimed priority to the '006 application – meaning, the patentability of the '137 application would be evaluated as though it were filed a year earlier. The examiner required the Wyeth applicants to amend certain claims in light of prior art. On August 5, 1997, the examiner issued a notice of allowance for the amended claims. Despite the notice of allowance, the Wyeth applicants abandoned the '137 application.

c. Wyeth's '328 Application

46. On November 5, 1997, the Wyeth applicants filed a continuation-in-part application, No. 08/964,328 (" '328 application"). A continuation-in-part

application repeats most of an earlier parent application but adds information that was not disclosed in the previous application. A continuation-in-part application must be filed while the earlier application is still pending.

47. The '328 application claimed priority to the '137 application and the '006 application. The examiner allowed some claims and rejected others in light of prior art. On February 16, 2000, the Wyeth applicants abandoned the '328 application – including the allowed claims.

d. Wyeth's '629 Application and the '171 Patent

48. On January 20, 2000 – one month before abandoning the '328 application – the Wyeth applicants filed a continuation-in-part application, No. 09/488,629 (" '629 application") that claimed priority to the '328 application, the '137 application, and the '006 application. The examiner allowed some claims and rejected others. The Wyeth applicants canceled one claim, amended other claims, and added new claims. The examiner allowed the claims (as amended).

49. On August 14, 2001, the '629 Application issued as U.S. Patent No. 6,274,171 B1 (" '171 patent"). The '171 patent contains 25 claims in total, including claims for (i) an extended release form of venlafaxine hydrochloride with spheroids, (ii) independent method of use claims for decreasing the incidence of nausea and vomiting, and (iii) independent method of use claims for minimizing

the troughs and peaks in drug concentration in patient's blood plasma. The '171 patent expires on March 20, 2017.

e. Wyeth's '412 Application and the '958 Patent

50. On June 19, 2001 – two months prior to the issuance of the '171 patent – the Wyeth applicants filed a divisional application, No. 09/884,412 (" '412 application). A divisional application is an application for an independent or distinct invention disclosing and claiming (only) a portion of the subject matter disclosed in an earlier application. The '412 application claimed priority to the '629 application (which resulted in the '171 Patent), the '328 application, the '137 application, and the '006 application. The examiner rejected some claims and allowed others. The Wyeth applicants then canceled one claim and added new claims that were substantially similar to claims issued in the '171 patent.

51. On July 16, 2002, the '412 Application issued as U.S. Patent No. 6,419,958 B2 (" '958 patent"). The '958 patent includes claims for (i) methods of use to decrease the incidence of nausea and vomiting and (ii) methods of use for minimizing the troughs and peaks in drug concentration in patient's blood plasma. The '958 patent included a terminal disclaimer that Wyeth did not seek an additional time period of patent protection beyond that afforded by the '171 patent – that is, through March 20, 2017.

f. Wyeth's '965 Application and the '120 Patent

52. On September 12, 2001, Wyeth filed a continuation application, No. 09/950,965 (" '965 application") that claimed priority to the '412 application (which resulted in the '958 patent), the '629 application (which resulted in the '171 patent), the '328 application, the '137 application, and the '006 application. The examiner rejected some claims and allowed others. Wyeth amended some claims to overcome the rejections. The examiner allowed the amended claims.

53. On June 11, 2002, the '965 application issued as U.S. Patent No. 6,403,120 B1 (" '120 Patent). The '120 patent contains 14 claims, all reciting a method of use for reducing the incidence of nausea and vomiting. The '120 patent also expires on March 20, 2017.

2. The Nausea Fraud: Wyeth Fraudulently Claimed Clinical Data Showed a Reduction in Nausea and Emesis

a. Wyeth Claimed Effexor XR Significantly Reduced the Incidence of Nausea and Emesis Associated with Effexor

54. In order to obtain a patent that protects a specific method of using a product, the applicants must have a legitimate basis for claiming that the method actually accomplishes what the applicants claim it accomplishes. That is, the applicants cannot just claim a method of using a pharmaceutical that reduces nausea; applicants must have a basis for claiming that the method of use reduces nausea and the method of use must actually reduce nausea.

55. In the original '006 provisional application, the Wyeth applicants claimed its patentable invention related to a 24-hour extended release dosage formulation of venlafaxine that "provides a lower incidence of nausea and vomiting than the conventional tablets." Specifically, the Wyeth applicants told the PTO that the use of the once-a-day formulation of venlafaxine hydrochloride capsules (later marketed as Effexor XR) reduced "the level of nausea and incidence of emesis that attends the administration of multiple daily dosing."

56. In support of this statement, the Wyeth applicants claimed clinical data showed that the incidence of nausea in people taking *extended release* venlafaxine was significantly less than in patients taking *instant release* venlafaxine:

> In clinical trials of venlafaxine hydrochloride ER, the probability of developing nausea in the course of the trials was greatly reduced after the first week. Venlafaxine ER showed a statistically significant improvement over conventional venlafaxine hydrochloride tablets in two eight-week and one 12 week clinical studies.

57. The Wyeth applicants made the same claim, repeating the *exact same* language, in the specifications accompanying the '137 application, the '328 application, the '629 application, the '412 application, and the '965 application. The *exact same* language appears in the '171 patent, the '958 patent, and the '120 patent.

58. The Wyeth applicants claimed that in light of the clinical data, it was entitled to method of use patents for the reduction in the incidence of nausea and emesis (vomiting):

> Thus, in accordance with this use aspect of the invention there is provided a method for reducing the level of nausea and incidence of emesis attending the administration of venlafaxine hydrochloride which comprises dosing a patient in need of treatment with venlafaxine hydrochloride with an extended release formulation of venlafaxine hydrochloride once a day in a therapeutically effective amount.

59. The Wyeth applicants made the same claim, repeating the *exact same* language, in the specifications accompanying the '137 application, the '328 application, the '629 application, the '412 application, and the '965 application. The *exact same* language appears in the '171, '958, and '120 patent specifications.

60. The Wyeth applicants did not provide the PTO with any other evidence of Effexor XR's ability to reduce the incidence of nausea or vomiting. Wyeth did not disclose to the PTO which studies showed the reported reductions; nor did Wyeth disclose to the PTO the raw data collected in these studies. Wyeth's sole support for its method of use claim for the reduction of vomiting and emesis was the express representation that two eight week and one twelve week clinical studies showed that Effexor XR "showed a statistically significant improvement" in the incidence of nausea and emesis over conventional Effexor.

b. The Clinical Data Did Not Show That Effexor XR Significantly Reduced the Incidence of Nausea and Emesis

(1) None of the Three Studies Showed a Reduction in Nausea or Emesis

61. The Wyeth applicants repeatedly told the PTO that "Venlafaxine ER showed a statistically significant improvement over conventional venlafaxine hydrochloride tablets in two eight-week and one 12 week clinical studies." The Wyeth applicants first made this statement in its March 25, 1996 '006 provisional application. It was not until nine years later – four years after securing the first method of use patent and in the context of patent infringement litigation with generic companies – that Wyeth first identified the "two eight week and one 12 week studies:" "600B-208-US," "600B-209-US," and "600B-367-EU," or studies 208, 209, and 367. Wyeth relied on these studies in seeking FDA approval of Effexor XR, but never identified them to the PTO.

62. Study 208 was a double-blind, flexible dose, twelve week efficacy study of Effexor XR, Effexor, and placebo in outpatients with major depression.

63. Study 209 was a double-blind, flexible dose, eight week study of Effexor XR and placebo in outpatients with major depression. Study 209 did not use instant release Effexor as a comparator.

64. Study 367 was a double-blind, flexible dose, eight-week efficacy study of Effexor XR, the competing antidepressant Paxil, and placebo in

outpatients with major depression. Study 367 did not use instant release Effexor as a comparator.

65. None of these three clinical studies showed that Effexor XR had a statistically significant improvement in the incidence of nausea over Effexor.

66. Studies 209 and 367 could not possibly have shown a reduction in nausea and emesis over conventional venlafaxine hydrochloride (Effexor) *because they did not include a group of patients taking instant release, conventional, Effexor*. Only study 208 included both patients receiving Effexor XR and patients receiving Effexor. Only study 208 could have allowed Wyeth to compare the incidence of nausea between the Effexor and Effexor XR groups.

67. But study 208 did not show a "statistically significant improvement" over Effexor. In fact, according to a published article describing the study, *the incidence of nausea was exactly the same in the Effexor XR and the Effexor groups*: 45% of Effexor XR patients experience nausea, as compared to 45% of Effexor patients. *See* Lynn M. Cunningham et al., *Once-Daily Venlafaxine Extended Release (XR) and Venlafaxine Immediate Release (IR) in Outpatients with Major Depression*, 9(3) ANNALS OF CLINICAL PSYCHIATRY 157 (1997) (reporting results of the venlafaxine XR 208 study group). Wyeth never disclosed this article (published years before the method of use patents issued) or its conclusions about rates of nausea to the PTO in any of its patent applications.

68. Study 208 also suffered from serious data corruption. The principal investigator of one of the study sites, Bruce Diamond Ph.D., and one of his subinvestigators, Richard Borison, M.D., Ph.D., were indicted for diversion of research funds on February 19, 1997, almost a full year after Wyeth claimed clinical data showed a significant reduction in the incidence of nausea with Effexor XR based in part of the results of study 208. Upon learning of these indictments, the FDA noted that the data from study 208 was "of uncertain reliability" and asked Wyeth to reanalyze the data from study 208, excluding the data from the corrupted site. Wyeth provided a reanalyzed data to the FDA. Wyeth never informed the PTO about the corrupted data. Wyeth never provided reanalyzed data – or any data from study 208 – to the PTO.

69. In September 2004, Wyeth submitted a further revised version of the final clinical report for the 208 Study. Although characterized as "minor corrections", the revisions included two revised analyses of the data on nausea. These revised analyses were never submitted to the PTO.

(2) Pooled Study Data Did Not Show a Reduction in Nausea or Emesis

70. The Wyeth applicants told the PTO that *each* of the three studies *independently* showed a statistically significant improvement in the incidence of nausea and emesis. Wyeth later claimed, in litigation with the generics, that it had not intended to claim the studies independently showed these results, but that

"pooled" data showed the professed reduction in nausea and emesis. But even if the data from all three studies were combined, or "pooled," it does not show a statistically significant reduction in the incidence of nausea or emesis.

71. First, because two of the studies did not include an Effexor treatment group, at best the data from the Effexor XR treatment groups in studies 208, 209, and 367 could be pooled and compared only to the conventional Effexor treatment group in study 208. This type of comparison is scientifically inappropriate, and cannot support a claim that one drug has fewer instances of side effects than another drug (particularly in light of the problems with the data from study 367, discussed below). The combination or "pooling" of patient data from studies 208, 209, and 367 would be statistically biased, and thus an improper basis for reaching a conclusion that there is a statistically significant improvement in nausea by patients taking Effexor XR as compared to patients taking instant release Effexor.

72. Second, even if this inappropriate pooling is done, it does not show a statistically significant difference in nausea and emesis.

73. At the time in 1996, when the Wyeth applicants submitted the original '006 application, Wyeth had not "pooled" the data from the 208, 209, and 367 studies. A decade later, during patent infringement litigation with the generics, Wyeth tried to cover its tracks by having 30(b)(6) deposition witnesses (Dr. Mangano and Dr. Alaburda) present new, never-before seen, elaborate calculations

and permutations of the original clinical study data that purportedly showed a diminished incidence of nausea and emesis. These calculations were done ten years after the clinical studies were completed and nine years after the Wyeth applicants told the PTO that extended release venlafaxine reduced the incidence of nausea.

74. Drs. Mangano and Alaburda testified that, according to yet another Wyeth employee, Wilfredo Ortega-Leone, the Wyeth applicants' claim that Effexor XR reduced the incidence of nausea was based on pooling the nausea data for the Effexor XR treatment groups in studies 208, 209, and 267 and comparing that data to nausea data for conventional Effexor treatment groups in entirely different (undisclosed) studies. Comparing different treatment groups from entirely different studies is wholly inappropriate, statistically biased, and is not a legitimate basis for claiming that one drug has fewer side effects than another drug. More importantly, Wyeth never disclosed its statistical slight-of-hand to the PTO.

75. In fact, the only reason that pooled Effexor XR data might possibly have shown a reduction in nausea (as compared to unrelated study data for conventional Effexor) is because it included the results of study 367. Study 367 reported markedly fewer instances of nausea in the Effexor XR treatment group than were reported by the Effexor XR treatment groups in Studies 208 and 209. Study 367 was conducted in Europe. Studies 208 and 209 were conducted in the

United States. Using the same extended release formulation, the European population in the 367 Study reported a 17% incidence of nausea, while the U.S. population in study 209 reported a 36% incidence of nausea.

76. The Wyeth applicants knew, and it was well known at the time, that the European population has a significantly greater tolerance for and/or underreports side effects such as nausea and vomiting than the U.S. population. By including the European XR data, it would look like Effexor XR reduced the incidence of nausea, when the real cause of the ostensible reduction in nausea was a known population difference. The Wyeth applicants did not disclose to the PTO that the claimed reduction in nausea and emesis was a result of studying populations that are less likely to experience and/or report side effects.

77. Further, as the FDA confirmed when analyzing Effexor XR's efficacy, *study 367 was a complete and utter failure:* "study 367 provided no persuasive evidence of antidepressant efficacy for venlafaxine ER." The Wyeth applicants never disclosed to the PTO that study 367 failed to show that Effexor XR was effective.

(3) The FDA Refused to Pool Side Effect Data From the 208, 209, and 367 Studies

78. In applying for FDA approval of Effexor XR, Wyeth argued that the FDA should evaluate the incidence of adverse events, including nausea, by pooling the data from studies 208, 209, and 367. The FDA disagreed.

79. On August 13, 1997, the FDA noted that "the incidence of many adverse events in the European study seemed to be substantially lower than in the two domestic studies" and determined that study 367 could not be included in the pooled data used to assess the adverse events associated with Effexor XR:

> The incidence of many important adverse events appeared to be lower in the European study (367) compared to both U.S. studies (208 and 209). Primarily for this reason, study 367 was not considered poolable with studies 208 and 209 for purposes of delineating the common adverse event profile of Effexor XR.

80. The FDA noted that including study 367's data in the pooled adverse event data would result in a marked reduction in the number of adverse events described on the drug's label. If data from studies 208, 209, and 367 were pooled, the Effexor XR label would have listed only eight common drug-related adverse events. In contrast, when only the data from studies 208 and 209 were pooled, the Effexor XR label would have listed an *additional* four common drug-related adverse events. The FDA stated that "Effexor XR is placed in a more favorable light if [Wyeth's proposed] pool is used," and therefore refused to allow the adverse event labeling to be based on Wyeth's proposed pooling.

81. Further, the FDA ultimately permitted Wyeth to pool data from the 208 and 209 studies, but not for the purpose of comparing the incidence of side effects between extended release venlafaxine and instant release venlafaxine. The FDA noted that "the pool of the two domestic studies [studies 208 and 209] allows

for a more conservative presentation of adverse event data in labeling and since Effexor XR will be marketing in the U.S., the pool of the two U.S. studies may be more relevant." The FDA's refusal to pool data from all three studies occurred only a year after Wyeth filed the original '006 application, well before Wyeth filed its subsequent patent applications, and almost 4 years before the first method of use patent issued.

82. Wyeth knew that including the results of European study 367 skewed the incidence of adverse events (including nausea) because the FDA told them so at least four years before the '171 patent issued, a patent whose claims were premised on Effexor XR's reported ability to reduce the incidence of nausea experienced by patients taking instant release Effexor. Yet the Wyeth applicants never informed the PTO that the FDA refused to include the data from study 367 when analyzing the incidence of adverse events associated with Effexor XR – that is, that the FDA refused to assess the incidence of side effects by pooling the 208, 209, and 367 data.

83. The FDA-approved package insert for Effexor XR, does not contain any representation that Effexor XR showed a statistically significant improvement in nausea over Effexor, even though the package insert compares Effexor XR and Effexor as to the potential for other adverse reactions in the course of their administration.

c. Wyeth Intended for the PTO to Rely on Its Material Misrepresentations

84. The Wyeth applicants intended to deceive the PTO with their misrepresentations about nausea.

85. The Wyeth applicants repeatedly made misrepresentations about the incidence of nausea associated with Effexor XR during the prosecution of the '137 Parent Application, the '328 Application, and each of the method of use patents. The Wyeth applicants affirmatively, and repeatedly, misrepresented that they possessed three clinical studies that showed Effexor XR significantly reduced the incidence of nausea and emesis associated with Effexor. The Wyeth applicants further affirmatively misrepresented that venlafaxine ER greatly reduced the probability of developing nausea. Specifically, the Wyeth applicants knowingly included the following sentences in the patent specifications submitted to the PTO:

> In clinical trials of venlafaxine hydrochloride ER, the probability of developing nausea in the course of the trials was greatly reduced after the first week. Venlafaxine ER showed a statistically significant improvement over conventional venlafaxine hydrochloride tablets in two eight-week and one 12 week clinical studies.

86. The Wyeth applicants knew these representations were false. The Wyeth applicants knew the only study directly comparing Effexor XR and Effexor (study 208) did not show the claimed statistically significant improvement. The Wyeth applicants knew Wyeth was not in possession of three clinical studies that

showed the claimed statistically significant improvement in nausea. The Wyeth applicants knew that two out of the three referenced studies did not even compare Effexor XR to Effexor. The Wyeth applicants knew that any claimed reduction in nausea and emesis was a result of conducting study 367 among a population that notoriously reports fewer side effects, such as nausea and emesis. Wyeth knew that the claimed reduction in nausea and emesis could only be supported, if at all, by inappropriately comparing different treatment groups across different studies. And, the Wyeth applicants knew the FDA had refused to pool the 208, 209, and 367 study data when analyzing the incidences of side effects associated with extended release venlafaxine.

87. The Wyeth applicants knew the PTO would read the patent specifications submitted with their various patent applications and thus receive their misrepresentations about Effexor XR's effectiveness in treating nausea and about the results of the three references clinical studies.

88. Each individual associated with the filing and prosecution of a patent application has a duty to disclose all information known to that individual to be material to patentability. 37 C.F.R. § 1.56. Information is material if it establishes unpatentability, whether by itself or in combination with other information, or if it refutes or is inconsistent with a position taken by an applicant in arguing for

patentability. The Wyeth applicants were aware of their individual obligations to disclose material information, and signed certifications acknowledging this duty.

89. The Wyeth applicants knew that their misrepresentations about nausea were material. No nausea method of use claims could have been patented in light of the truth: extended release venlafaxine did not meaningfully reduce the incidence of nausea, Wyeth did not have clinical data from three studies that showed a reduction in nausea, and pooled data from three studies did not show a reduction in nausea.

90. The Wyeth applicants also failed to inform the examiner about the Cunningham article (reporting results from study 208) and the FDA's refusal to pool the data. Both were material: a reasonable examiner would want to know about contradicting published materials and another agency's determination about pooling.

91. The Wyeth applicants knew there was a substantial likelihood the PTO would rely on their misrepresentations about nausea in evaluating their numerous nausea method of use claims because the Wyeth applicants did not provide any other evidence that extended release venlafaxine reduced nausea.

92. The PTO did, in fact, rely on the Wyeth applicants' misrepresentations. In the absence of any other basis for substantiating Wyeth's nausea claim, the PTO relied on the singular, but oft repeated, statement that

clinical studies showed Effexor XR reduced the incidence of nausea and emesis as compared to Effexor in approving *twenty* claims that began by reciting a method of use that reduces nausea and emesis:

> A method for providing a therapeutic blood plasma concentration of venlafaxine over a twenty four hour period with diminished incidence of nausea and emesis which comprises administering orally to a patient in need thereof ….

93. The nausea fraud directly affects claims 20, 22, and 23 of the '171 patent; claims 1, 3, and 4 of the '958 patent; and *all* of the claims of the '120 patent. Because Wyeth defrauded the PTO by claiming a reduction in nausea, Wyeth is not entitled to immunity for its petitioning activities in seeking the '171, '958, '120 patents.

3. The Unexpected Discovery Fraud: Wyeth Fraudulently Claimed It was the First to "Unexpectedly" Discover Extended Release Venlafaxine

94. An applicant can obtain a patent only if he is the first to invent the subject matter described in the patent application. If earlier publications or patents disclose the invention, or it can be established that someone else invented the subject matter, the invention is not patentable. *See* 35 U.S.C. § 102. Prior invention of the subject matter by someone else may be demonstrated by:

- Printed publications that describe the invention, either in the U.S. or internationally, before the patent applicant invented the invention (35 U.S.C. 102 § (a));

- A printed publication that describes the invention, published more than one year before the patent applicant filed a patent application for it (35 U.S.C. 102 § (b));
- A U.S. patent application filed by another inventor describing the invention before the patent applicant invented the invention (35 U.S.C. §102(e)); and
- Evidence of earlier invention by another, including non-public disclosures (35 U.S.C. § 102 (f); *OddzOn Products, Inc. v. Just Toys, Inc.*, 122 F.3d 1396, 1403 (Fed. Cir. 1997).

95. Throughout the prosecution of the method of use patents, the Wyeth applicants fraudulently misrepresented Wyeth's "unexpected" discovery of an extended release venlafaxine hydrochloride capsule to the PTO. *Wyeth represented in all of its applications for the method of use patents that it was "completely unexpected that an extended release formulation containing venlafaxine could be obtained."* The Wyeth applicants first made this representation in the provisional '006 application, filed on March 25, 1996. All of the method of use patents include this language, the last of which issued on July 16, 2002 (the '958 patent).

96. But an extended release version of venlafaxine was not at all unexpected to Wyeth. The Wyeth applicants were aware of extended release versions of venlafaxine before filing the '006 application. Wyeth's own Upton patent disclosed extended release venlafaxine. Wyeth also knew that Alza Corporation ("Alza") had filed an application to patent a version of extended release venlafaxine before Wyeth filed the '006 application.

97. The Wyeth applicants had multiple opportunities to amend the specifications in its various applications to no longer assert that extended release venlafaxine hydrochloride was surprising or unexpected and failed to do so. Wyeth knew that by making such an amendment, it would no longer be able to claim priority back to the date of the '006 application. Without the '006 application's priority date, Wyeth would not have been able to patent any version of Effexor XR.

a. Wyeth's Upton Patent Disclosed Extended Release Venlafaxine

98. Wyeth's own Upton patent disclosed extended release venlafaxine (*see supra*, ¶¶ 90-95). Wyeth applied for the Upton patent on January 30, 1995, more than a year before Wyeth claimed extended release venlafaxine was surprising in the '006 application. The Upton patent issued to Wyeth on April 9, 1996, one month after Wyeth filed the '006 provisional application and years before the method of use patents issued (August 2001 – July 2002). This disclosure makes an extended release formulation of venlafaxine not at all surprising, especially not to Wyeth.

99. The Upton patent qualifies as prior art under 35 U.S.C. §102(e) and 35 U.S.C. §102(f).

b. Alza's '589 PCT Application Disclosed Extended Release Venlafaxine

100. In 1992, Wyeth entered into an agreement with Alza to develop an extended release formulation of venlafaxine hydrochloride using Alza's proprietary drug delivery systems. Alza knew Wyeth was simultaneously developing an extended release version of venlafaxine in house.

101. The agreement granted Alza ownership rights in any information generated or acquired during the collaboration and the patents result from the collaboration. Alza also retained the right to use, disclose, and license information from the collaboration to third parties.

102. The collaboration agreement required Alza and Wyeth to exchange information about their respective efforts to develop extended release venlafaxine. The parties' Scientific Steering Committee, comprised of Alza and Wyeth employees, held one or more meetings that discussed the progress of the collaboration and other confidential information about the project, including the status of patent application filings and patent prosecution.

103. On May 27, 1993, Alza filed patent application U.S. Serial No. 08/068,480, listing inventors Edgren, *et. al* (the Edgren application). The Edgren application disclosed venlafaxine hydrochloride. The status of the prosecution of the Edgren application was discussed at multiple Scientific Steering Committee meetings between Wyeth and Alza, pursuant to the collaboration agreement. The

Edgren application eventually matured into U.S. Patent 6,440,457 on August 27, 2002 (the Edgren Patent).

104. On December 8, 1994, the World Intellectual Property Organization in Geneva, Switzerland published WO 94/27589, assigned to Alza (the '589 PCT application). The '589 PCT application claims priority to the Edgren application. The '589 PCT application discloses once-a-day venlafaxine extended release formulations, methods for the administration of venlafaxine extended release formulations, and the hours required for *in vitro* dissolution.

105. Alza sought to develop formulations that provided for a controlled rate of drug release over an extended period of time. As Alza explained in the '589 PCT application, conventional instant release formulations result in "large peaks and valleys … in the drug blood levels." The applicants stated that there was a "need for a controlled-release dosage form that can administer the drug at a controlled rate over an extended time to provide constant therapy and thereby eliminate the need for multiple dosing." The Alza formulations sought to "provide a drug delivery controlled release system that can deliver a drug for maintaining constant drug levels in the blood, thereby functioning as a controlled release system." Alza further sought "to provide a once a day controlled release dosage form to deliver [venlafaxine hydrochloride] orally to a patient in need of

therapy[,]" and "to provide a method for administering [venlafaxine hydrochloride] in a therapeutic range while simultaneously avoiding a toxic range[.]"

106. The '589 PCT application disclosed venlafaxine hydrochloride specifically as the antidepressant pharmaceutical ingredient. The formulations were to be administered once-a-day in a single dose over a twenty-four hour period. The '589 PCT application indicates that the dosage form successfully maintained constant drug levels in the blood by virtue of its extended release properties.

107. While the '589 PCT application and Edgren patent do not report peak blood plasma levels, minimization of the troughs and peaks of blood plasma level are inherent in the extended release formulations disclosed in the '589 PCT application and the Edgren patent. One can reasonably infer that the Alza Formulation for controlled release venlafaxine hydrochloride formulations eliminated peaks and troughs of drug concentration in a patient's blood plasma attending the therapeutic metabolism of plural daily doses of venlafaxine hydrochloride.

108. Both the Edgren patent and the '589 PCT application qualify as prior art to the method of use patents. The earliest date of invention for Wyeth's extended release formulations is March 25, 1996, the filing date of the '006 provisional application.

109. The '589 PCT application was published on December 8, 1994, over a year before Wyeth filed the '006 application. The '589 PCT application qualifies as prior art against the method of use patents as a printed publication published in a foreign country before Wyeth invented venlafaxine hydrochloride extended release. 35 U.S.C. 102(a). The '589 PCT application further qualifies as prior art against the method of use patents as printed publications published more than one year before Wyeth filed the '006 provisional application. 35 U.S.C. 102(b).

110. The Edgren application was filed with the PTO on May 27, 1993, roughly three years before Wyeth invented extended release venlafaxine hydrochloride (as claimed in the '006 Provisional Application). The Edgren inventors disclosed an extended release venlafaxine hydrochloride formulation that maintained a constant level of venlafaxine in a patient's plasma over a twenty-four period, which can reduce toxic effects. Thus, the Wyeth inventors are not the first to invent the broadly recited method of reducing toxic effects (such as nausea and emesis) or methods of eliminating the peaks and troughs (*i.e.*, maintaining a constant level) of drug in a patient's plasma over a twenty-four period. 35 U.S.C. § 102(f).

111. The Edgren patent qualifies as patent defeating prior art against the method of use patents as a patent application by another filed in the U.S. before

Wyeth invented its controlled release formulation for venlafaxine hydrochloride. 35 U.S.C. § 102(e).

c. Wyeth Intentionally Deceived the PTO by Fraudulently Claiming it Was the First to Discover, "Unexpectedly," Extended Release Venlafaxine

112. The Wyeth applicants withheld highly material information from the PTO with the intent to deceive the PTO. The Wyeth applicants had a duty to present all information that was known to be material to the patentability of the claims to the examiner. Information that is non-public, but known to the applicant, can be material to patentability. The Wyeth applicants breached their duty of candor to the PTO by failing to properly disclose Wyeth's collaboration agreement with Alza, the '589 PCT application, and the Edgren application.

113. Wyeth knew about the Edgren application and the '589 PCT application – prior to applying for and prosecuting the method of use patents – from its participation in the Scientific Steering Committee with Alza under the terms of their collaboration agreement.

114. The Wyeth applicants were aware that the '589 PCT application discloses "controlled release dosage forms" of venlafaxine hydrochloride. The Wyeth applicants were similarly aware the PCT application claimed priority back to May 27, 1993, well before Wyeth claimed to have invented its extended release venlafaxine. Wyeth and Wyeth Attorney Arthur G. Seifert disclosed the existence

of the '589 PCT Application to the PTO on an IDS sent to the PTO on August 13, 1998 during the prosecution of the '328 Application. (Wyeth did not disclose the '589 PCT Application during the prosecution of the earlier '137 application.)

115. Despite their knowledge of the disclosures in the '589 PCT Application, the Wyeth applicants each nonetheless continued to misrepresent to the PTO that "[i]t was completely unexpected that an extended release formulation containing venlafaxine hydrochloride could be obtained."

116. The collaboration agreement and the resulting '589 PCT application were material to patentability because they presented a *prima facie* case of invalidity as a prior invention of another. Wyeth inventors Sherman, Clark, Lamar and White were not the first to invent methods of (i) eliminating peaks and troughs of venlafaxine in a patient's blood plasma and (ii) reducing nausea and emesis, via once daily dosing of venlafaxine: *Alza and its scientists, with the knowledge and collaboration of Wyeth, had developed technology and filed and prosecuted a patent application directed to those methods at least three years before Wyeth made its "unexpected" discovery.* The Wyeth inventors derived at least part of their invention from the collaboration with Alza.

117. The '589 PCT application is separately material because, contrary to Wyeth's claims to discovery, it was not unexpected that one could make a

controlled release venlafaxine product that eliminated the peaks and troughs of the drug in blood plasma or reduce the incidence of nausea.

118. That the Wyeth applicants intended to deceive the PTO may be inferred from their knowledge that (1) Alza was developing an extended release version of venlafaxine, (2) Alza disclosed to Wyeth that it had filed the Edgren application and reported to Wyeth on the status of the Edgren application, (3) Wyeth was aware of the '589 PCT application (as evidenced by its late submission of the '589 PCT application to the PTO), and (4) Wyeth knew the '589 PCT application disclosed formulations of extended release venlafaxine that minimized the troughs and peaks of the amount of venlafaxine in patients' blood serum levels.

119. The Wyeth applicants' intent to deceive may also be inferred from Wyeth's financial motivation. Wyeth was aware of the impact that an Alza patent would have on Wyeth's exclusivity to sell Effexor XR. Wyeth knew that the collaborative agreement provided that Alza would own the rights to any patent that resulted from their collaboration. Alza was free to sell use or license the rights to the technology to a third party. Even a patent that named both Wyeth and Alza inventors would be at least co-owned, if not completely owned, by Alza. Wyeth would no longer have a monopoly over extended release venlafaxine.

120. The level of intent in withholding the full scope of the Alza formulations while repeatedly arguing through six patent applications that the Wyeth discovery was unexpected shows a high level of intent to deceive the PTO.

121. Wyeth's unexpected discovery fraud directly affects claims 20-25 of the '171 patent and all of the claims of the '958 and '120 patents. And in the stark light of later patent infringement litigation, all three patents would be rendered entirely invalid and unenforceable as a result of the prior rejection fraud.

4. The Prior Rejection Fraud: Wyeth Failed to Disclose a Previous Examiner's Rejection of all Method of Use Claims in Light of Wyeth's Own Upton Patent.

a. Wyeth Failed to Disclose its Own Upton Patent to the Original Patent Examiner

122. On January 30, 1995, more than a year before the Wyeth applicants filed the '006 application, the Wyeth applicants filed patent application no. 08/380,093, by Upton *et al.* (the Upton application). Because Wyeth defrauded the PTO by claiming it was the first to "unexpectedly" discover extended release venlafaxine, Wyeth is not entitled to immunity for its petitioning activities in seeking the '171, '958, and '120 patents. The Upton application sought a patent for a method of using venlafaxine to treat hypothalamic amenorrhea (menopause) in non-depressed women. It did not seek approval of any formulations of venlafaxine, and it is not apparent from the face of the specification itself that it would reference any particular formulations of venlafaxine. But included in the

fine print of the proposed patent specification was a single reference to a "sustained oral administration form or time-release form [of venlafaxine], which may be used to spread the dosage over time, such as for once-a-day applications."

123. On March 4, 1996, the PTO mailed Wyeth a Notice of Issue, informing Wyeth that the Upton application would issue as a patent. Wyeth had drafted the Upton application, and the Wyeth applicants were fully aware the Upton patent disclosed once a day venlafaxine formulations that "spread the dosage over time." Wyeth rushed to file a provisional application that covered nausea and "troughs and peaks" claims (discussed below) to avoid the Upton Patent standing as prior art to future extended release venlafaxine claims. On March 26, 1996, a mere 22 days after getting notice the Upton patent would issue, the Wyeth applicants filed the '006 application.

124. On April 9, 1996, less than one month after the '006 provisional application was filed, the Upton application issued as U.S. Patent No. 5,506,270 (the Upton patent). The Upton patent was assigned to Wyeth. The Upton patent contained the same reference to sustained and time release forms of venlafaxine as the proposed specification at column 5, lines 23-27:

> It is understood that … this invention is intended to cover any means of administration to a patient of an active amount of the compounds listed above in the treatment of hypothalamic amenorrhea. Such administrations may also be provided in a bolus form, intermittent-release form, sustained oral administration form or time-release

> form, which may be used to spread the dosage over time, such as for once-a-day applications.

125. This disclosure of extended release venlafaxine formulations is prior art relevant to claims made in the applications for the method of use patents. This prior art renders other method of use claims related to spreading the dose over time (such as once-a-day dosing) and obvious consequences of spreading the dose over time (such as minimizing the "troughs and peaks" of venlafaxine in the blood and reducing nausea thought to be associated with increased levels of venlafaxine in the blood) unpatentable.

126. The Wyeth applicants knew the Upton patent disclosed extended release venlafaxine. The Wyeth applicants knew this information was material. The Wyeth applicants also knew that a reasonable examiner would want to know (i) that Wyeth had been prosecuting (for over a year) a patent application for a method of use for venlafaxine whose specification disclosed extended release venlafaxine, (ii) that a prior examiner had rejected the claims, and (iii) that Wyeth had *agreed* with that objection.

b. Examiner Hulina Rejected Wyeth's Independent Method of Use Claims for an Extended Release Venlafaxine in Light of the Upton Patent

127. On March 20, 1997, almost a year after Wyeth's Upton patent issued, the Wyeth applicants filed the '137 application, claiming priority to the '006 application. The '137 application was assigned to Examiner Amy Hulina.

128. Claim 1 recited an extended release formulation of venlafaxine hydrochloride with spheroids:

> 1. An encapsulated, extended release formulation of venlafaxine hydrochloride comprising a hard gelatin capsule containing a therapeutically effective amount of spheroids comprised of venlafaxine hydrochloride, microcrystalline cellulose and hydroxypropylmethylcellulose coated with ethyl cellulose and hydroxypropylmethylcellulose.

129. Claim 9 recited a method of use for reducing incidences of nausea and vomiting associated with venlafaxine:

> 9. A method for providing a therapeutic blood plasma concentration of venlafaxine over a twenty four hour period with diminished incidences of nausea and emesis which comprises administering orally to a patient in need thereof, an encapsulated, extended release formulation that provides a peak blood plasma level of venlafaxine in from about four to about eight hours, said formulation containing venlafaxine hydrochloride as the active ingredient.

130. Claim 10 recited a method of use for reducing the disparities in concentration of venlafaxine in a patient's blood serum:

> 10. A method for eliminating the troughs and peaks of drug concentration in a patient's blood plasma attending the therapeutic metabolism of plural daily doses of which comprises administering orally to a patient in need thereof, an encapsulated, extended release formulation that provides a peak blood plasma level of venlafaxine in from about four to about eight hours, said formulation containing venlafaxine hydrochloride as the active ingredient.

131. On July 10, 1997, the Wyeth applicants submitted an Information Disclosure Statement ("IDS") listing five U.S. Patents, no foreign patents, and no other publications. Wyeth did not list the original compound patent (Husbands) on the IDS, but referenced it in the specification. Examiner Hulina considered all 5 references reported by Wyeth. *The Wyeth applicants did not list or otherwise disclose the Upton patent.*

132. Examiner Hulina discovered Wyeth's Upton patent in her prior art search.

133. During a telephone interview on July 30, 1997, Examiner Hulina informed Wyeth applicant Attorney Robert Boswell that independent claims 9 and 10, the nausea and "troughs and peaks" method of use claims, were not patentable as independent claims in light of the disclosure of extended release formulations of venlafaxine in the Upton patent. She further informed Attorney Boswell that these method of use claims would only be patentable if Wyeth amended them to depend on the particular formulation of extended release venlafaxine in claim 1.

134. The Wyeth applicants had hoped to patent independent method of use claims, claims unassociated with a particular formulation of extended release venlafaxine, in order to maximize a market exclusivity for extended release venlafaxine hydrochloride capsules. Independent method of use claims could be asserted against any generic manufacturer that attempted to market any

formulation of extended release venlafaxine. But Wyeth could only assert dependent method of use claims against a generic manufacturer that happened to be using the exact same formulation of extended release venlafaxine that the method of use claims depended on. Independent method of use claims would provide further impediments to generic manufacturers and could translate into millions more dollars in Wyeth's pockets.

135. The Wyeth applicants did not challenge Examiner Hulina's conclusion that claims 9 and 10 were unpatentable as independent claims. Rather, Wyeth applicant Attorney Boswell agreed with the Examiner's conclusion by authorizing the examiner to amend the method of use claims in order to avoid rejection. An examiner's amendment changed Claims 9 and 10 from independent claims to dependent claims, thereby limiting the method of use claims to the specific extended release formulation of venlafaxine hydrochloride recited in claim 1, and acknowledging that stand alone method of use claims were not patentable in light of the Upton patent.

136. On August 5, 1997, Examiner Hulina issued a notice of allowance for the amended, now dependent, method of use claims and the independent formulation claim, noting that "[t]he prior art does not teach or suggest the specific extended release claim *formulation* according to claim 1" (emphasis added) Despite the notice of allowance, the Wyeth applicants decided to abandon the '137

application – presumably in the hopes that a new application might draw a different examiner that would be unfamiliar with the Upton patent's disclosure of extended release venlafaxine and would, therefore, allow independent nausea and "troughs and peaks" method of use claims.

c. Wyeth Never Discloses that the PTO Rejected its Method of Use Claims in Light of the Upton Patent

(1) Wyeth Did Not Disclose the Previous Examiner's Rejection in the '328 Application

137. On November 5, 1997, the Wyeth applicants filed the '328 continuation-in-part application. Fortunately for Wyeth, the '328 application was assigned to a different Examiner in a different art unit, James M. Spear in Art Unit 1615.

138. Claim 1 recited a formulation claim similar to claim 1 in the '137 application, an extended release form of venlafaxine hydrochloride with spheroids. Independent method of use claims 13 and 14 were identical to proposed method of use claims 9 and 10 of the abandoned '137 application – claims explicitly rejected by Examiner Hulina in light of the Upton patent's reference to an extended release form of venlafaxine hydrochloride, that "spread the dosage over time," claims the Wyeth applicants had agreed to amend, and claims that Examiner Hulina had allowed once amended. The '328 application did not contain any other independent method of use claims.

139. On February 9, 1998, the Wyeth applicants submitted an IDS identifying the same five U.S. Patents identified in the IDS for the '137 application as well as the Upton and Husbands patents. No foreign patent documents or other publications were listed. Examiner Spear considered all of the references on the IDS. On August 13, 1998, the Wyeth applicants submitted a Supplemental IDS, listing three foreign patent documents. Examiner Spears also considered the new submissions.

140. On October 14, 1998, Examiner Spear allowed the method of use claims (claims 13 and 14) to issue as independent claims – the very claims that Examiner Hulina had previously required Wyeth to amend to be dependent on a particular formulation. The Wyeth applicants never informed Examiner Spear that the Upton patent identified the existence of an extended release formulation of venlafaxine hydrochloride that rendered their method of use claims unpatentable. The Wyeth applicants never disclosed to Examiner Spear that they had previously *agreed* to amend the *very same claims* to be dependent claims. And the Wyeth applicants never disclosed to Examiner Spear that a previous Examiner had found the exact same claims to be unpatentable.

141. That the Upton patent references a sustained release, once-a-day formulation of venlafaxine is not evident from the title of the patent: "Venlafaxine in the Treatment of Hypothalmic Amenorrhea in Non-Depressed Women."

Similarly, the reference to a sustained release formulation is contained in a single sentence in the middle of a three page single-spaced specification; an examiner would have to review the Upton patent very closely to find the reference that the Wyeth applicants were all too well aware of.

142. Also on October 14, 1998, Examiner Spear *rejected* claim 1, for a formulation with spheroids, as unpatentable in light of prior art (other than the Upton patent). The Wyeth applicants responded to examiner's rejections by canceling, amending and adding new claims. On July 21, 1999, Examiner Spear rejected the new claims, stating that the Applicants' arguments to overcome the prior art were not persuasive. The Wyeth applicants responded by filing a petition for an extension of time, but never ultimately responded. On February 16, 2000, the Wyeth applicants abandoned the '328 Application – including its allowed independent method of use claims.

(2) Wyeth Did Not Disclose the Previous Examiner's Rejection in the '629 Application

143. On January 20, 2000, a month before abandoning the '328 application, the Wyeth applicants filed the '629 continuation-in-part application. Wyeth's latest application was again assigned to Examiner Spear.

144. The '629 application contained a nearly identical specification to the '328 application. Claim 1, again, recited an extended release version of venlafaxine hydrochloride in spheroids that was substantially similar to the claim

rejected by Examiner Spear during the prosecution of the '328 application in light of the prior art. Claims 21 and 22, again, recited the same independent method of use claims originally presented in (rejected) claims 9 and 10 of the '137 application and (allowed but abandoned) claims 13 and 14 in the '328 application:

> 21. A method for providing a therapeutic blood plasma concentration of venlafaxine over a twenty four hour period with diminished incidences of nausea and emesis which comprises administering orally to a patient in need thereof, an encapsulated, extended release formulation that provides a peak blood plasma level of venlafaxine in from about four to about eight hours, said formulation containing venlafaxine hydrochloride as the active ingredient.
>
> 22. A method for eliminating the troughs and peaks of drug concentration in a patient's blood plasma attending the therapeutic metabolism of plural daily doses of which comprises administering orally to a patient in need thereof, an encapsulated, extended release formulation that provides a peak blood plasma level of venlafaxine in from about four to about eight hours, said formulation containing venlafaxine hydrochloride as the active ingredient.

145. The Wyeth applicants, again, never informed Examiner Spear that the Upton patent identified the existence of an extended release formulation of venlafaxine hydrochloride that rendered their method of use claims unpatentable. The Wyeth applicants, again, never disclosed that it had agreed to amend these claims to be dependent claims in order to avoid a rejection over the prior art disclosed by Wyeth's own Upton patent. The Wyeth applicants, again, never

disclosed to Examiner Spear that a previous Examiner determined these claims were unpatentable. On January 4, 2001, Examiner Spear allowed claims 21 and 22.

146. The Wyeth applicants then added additional method of use claims 23-26. Claims 23 and 24 recite methods of use "with diminished incidence of nausea." Claims 25 and 26 recite methods of use for "eliminating the troughs and peaks of drug concentration in a patient's blood plasma." All are substantially similar to the method of use claims rejected by Examiner Hulina. Nonetheless, in the absence of Wyeth's disclosure of her rejection and failing to directing the examiner to Upton's fleeting reference to extended release venlafaxine, Examiner Spear allowed these independent method of use claims.

147. On August 14, 2001, the '629 Application issued as the '171 patent. The '171 patent contains six independent method of use claims: claims 20 through 25. All recite either diminished incidences of nausea or eliminating the troughs and peaks in a patient's blood plasma. (Due to renumbering, proposed claims 21 and 22 issued as claims 20 and 21. Proposed claims 23 through 26 issued as claims 22 through 25).

(3) Wyeth Did Not Disclose the Previous Examiner's Rejection in the '412 Application

148. On June 19, 2001, two months before the '171 patent issued, the Wyeth applicants filed the divisional '412 application to pursue rejected claim 1 of the '629 application. The application was again assigned to Examiner Spear.

149. The specification and claims of the '412 application were identical to the '629 application. The Wyeth applicants then canceled claims 2-22 and added new, independent method of use claims 23 and 24:

> 23. A method for providing a therapeutic blood plasma concentration of venlafaxine over a twenty four hour period with diminished incidences of nausea and emesis which comprises administering orally to a patient in need thereof, an extended release formulation that provides a peak blood plasma level of venlafaxine in from about four to about eight hours, said formulation containing venlafaxine hydrochloride as the active ingredient.
>
> 24. A method for eliminating the troughs and peaks of drug concentration in a patients blood plasma attending the therapeutic metabolism of plural daily doses of which comprises administering orally to a patient in need thereof, an extended release formulation that provides a peak blood plasma level of venlafaxine in from about four to about eight hours, said formulation containing venlafaxine hydrochloride as the active ingredient.

150. Claims 23 and 24 are substantially the same method of use claims originally presented in (rejected) claims 9 and 10 of the '137 application and allowed claims 20 and 21 of the '171 patent, differing only by no longer including the word "encapsulated." The Wyeth applicants, again, never informed Examiner

Spear that the Upton patent identified the existence of an extended release formulation of venlafaxine hydrochloride that rendered their method of use claims unpatentable. The Wyeth applicants, again, never disclosed to Examiner Spear that a previous Examiner determined method of use claims substantially similar to claims 23 and 24 were unpatentable. The Wyeth applicants, again, never disclosed that it had agreed to amend substantially similar claims in order to avoid a rejection over the prior art disclosed by Wyeth's own Upton patent.

151. On January 13, 2002, Examiner Spear rejected claims 23, and 24 as being unpatentable over claims 20 and 21 of the '171 Patent. The Wyeth applicants contested that claims 23 and 24 were obvious in light of the '171 patent, but filed a terminal disclaimer confirming that it did not, and would not, seek an additional time period of patent protection beyond that afforded by the '171 patent.

152. The Wyeth applicants also added claims 25 through 28, additional independent method of use claims. Claims 25 through 28 either recite a method of use "with diminished incidence of nausea" or for "eliminating the troughs and peaks of drug concentration in a patient's blood plasma." All are substantially similar to the method of use claims rejected by Examiner Hulina. Nonetheless, in the absence of the appropriate disclosures by Wyeth, Examiner Spear allowed claims 23 through 28.

153. On July 16, 2002, the '412 application issued as the '958 patent. The '958 patent contains six method of use claims: claims 1-6. All related to either diminished incidences of nausea or eliminating the troughs and peaks in a patient's blood plasma. (Due to renumbering, proposed claims 23 and 24 issued as claims 1 and 2. Proposed claims 25 through 28 issued as claims 3 through 6.)

(4) Wyeth Did Not Disclose the Previous Examiner's Rejection in the '965 Application

154. On September 12, 2001, the Wyeth applicants filed the '965 continuation-in-part application. The '965 application was, again, assigned to Examiner Spear.

155. The '965 application contained the same specification and claims as the '412 application (and corresponding '958 patent). The Wyeth applicants canceled claims 2-22 and added new claims 23-34. Claim 23 recited a method of use claim for diminished incidences of nausea, and substantially similar to rejected claim 9 of the '137 application:

> 23. A method for providing a therapeutic blood plasma concentration of venlafaxine over a twenty four hour period with diminished incidences of nausea and emesis which comprises administering orally to a patient in need thereof, an extended release formulation that provides a peak blood plasma level of venlafaxine of no more than 150 ng/ml, said formulation containing venlafaxine hydrochloride as the active ingredient.

156. The Wyeth applicants, again, never disclosed to Examiner Spear that a previous Examiner determined a claim substantially similar to claim 23 was unpatentable. The Wyeth applicants, again, never disclosed that it had agreed to amend a substantially similar claim in order to avoid a rejection over the prior art disclosed by Wyeth's own Upton patent. And the Wyeth applicants did not direct the examiner to Upton's reference to extended release venlafaxine hydrochloride.

157. Examiner Spear allowed claim 23, and objected to claims 24-34. The Wyeth applicants later amended claims 24 and 25 to depend from allowed claim 23. Examiner Spear allowed the amended claims.

158. On June 11, 2002, the '965 application issued as the '120 Patent. Due to renumbering, proposed claim 23 issued as claim 1:

> 1. A method for providing a therapeutic blood plasma concentration of venlafaxine over a twenty four hour period with diminished incidences of nausea and emesis which comprises administering orally to a patient in need thereof, an extended release formulation that provides a peak blood plasma level of venlafaxine of no more than 150 ng/ml, said formulation containing venlafaxine hydrochloride as the active ingredient.

159. All other claims depended from claim 1.

d. Wyeth Intentionally Committed Fraud on the PTO by Failing to Disclose Material Information

160. The prosecution history of the '137 Parent Application shows that Examiner Hulina judged the independent method of use claims (claims 9 and 10)

unpatentable in view of the prior art taught by Wyeth's Upton patent. Claims 9 and 10 became patentable only after Wyeth amended the claims to be dependent on a particular formulation of extended release venlafaxine at the insistence of Examiner Hulina.

161. Throughout the prosecution history of the method of use patents (including the '328 application, the 412 application, and the '629 application), Wyeth failed to both (i) inform Examiner Spear that the Upton patent identified the existence of an extended release formulation of venlafaxine hydrochloride that rendered their method of use claims unpatentable and (ii) disclose material information relating to Examiner Hulina's determination of unpatentability.

162. The Wyeth applicants had a duty to disclose all information material to patentability, including information that by itself renders the claims unpatentable. The Wyeth applicants failed to disclose to new Examiner Spear the contrary findings of the earlier examiner on the identical claims. The Wyeth applicants failed to disclose the basis of the earlier examiner's contrary findings – that a prior art patent owned by Wyeth itself taught an extended release formulation of venlafaxine. The Wyeth applicants failed to disclose to Examiner Spear the fact that they had already agreed to narrow the scope of identical claims in order to avoid a rejection over Wyeth's own prior art patent – the Upton Patent. The Wyeth applicants failed to disclose to Examiner Spear the fact that once they

had agreed to amend the claims to overcome the prior art reference, that Examiner Hulina found the claims patentable and issued a Notice of Allowability.

163. The information withheld by the Wyeth applicants was material. This information is of the type a reasonable examiner would want to know, as it directly impacts the patentability of the claims.

164. The Wyeth applicants withheld this material information and thereby breached their duty of disclosure to the PTO. They did so in order to avoid prior art rendering independent method of use claims unpatentable; that is, the Wyeth applicants sought to prosecute independent method of use claims that were substantially similar to the previously rejected independent method of use claims.

165. The Wyeth applicants withheld this material information with intent to mislead or deceive the PTO. Intent to deceive the Patent Office can be inferred by refiling claims that had been previously rejected. Wyeth knowingly, repeatedly, presented unpatentable and previously rejected claims to the examiner on multiple occasions.

166. The Wyeth applicants failed to amend the independent method of use claims in accordance with Examiner Hulina's findings in the subsequent patent applications. The Wyeth applicants had multiple opportunities to amend claims during prosecution of the method of use patents, and in fact did amend claims

several times. But the Wyeth applicants never made the necessary amendments to overcome patent-defeating prior art on identically or substantially similar claims.

167. The Wyeth applicants had multiple opportunities to correct the record and bring the rejection of the claims based on the Upton Patent to the attention of Examiner Spear, yet failed to do so. The Wyeth applicants amended the claims several times in each subsequent application; Wyeth amended the specifications of two subsequent applications (the '328 application and the '629 application, which issued as the '171 patent) and amended the inventorship of the '629 application. Each filing presented an opportunity for Wyeth to correct the record, but it failed to do so.

168. Intent to deceive the Patent Office can be inferred by the numerous opportunities that Wyeth had to amend claims and specifications and/or bring the prior decision of unpatentability to Examiner Spears' attention. Based upon reasonable inference, Wyeth intentionally failed to disclose all pertinent information that was known to them during prosecution of the '171, '120, and '958 patents with an intent to deceive the PTO.

169. But for this fraud on the PTO, no independent nausea or "troughs and peaks" method of use claims would have issued in the method of use patents. Specifically, Wyeth's prior rejection fraud affects claims 20 through 25 of the '171 patent and all of the claims of the '958 and '120 patents. Because Wyeth

defrauded the PTO by failing to disclose (i) the previous examiners' rejection, Wyeth is not entitled to immunity for its petitioning activities in seeking the '171, '958, and '120 patents. In the stark light of later patent infringement litigation, all three patents would be rendered entirely invalid and unenforceable as a result of the prior rejection fraud.

5. The Inderal Fraud: Wyeth Failed to Disclose that It Developed its Effexor XR Formulation by Merely Substituting Venlafaxine for the Active Ingredient of its Inderal LA Product.

a. Wyeth Did Not Disclose that it Used the Formulation of Inderal LA to Develop Effexor XR.

170. Wyeth was selling Inderal LA years before it began its development of Effexor XR. Inderal LA is a sustained release formulation of propranolol which is used to treat high blood pressure.

171. Propranolol and venlafaxine have similar chemical properties. Both have similar molecular weights; both are formulated using the same salt; both are very soluble in water; and both have similar half-lives. In addition, the necessary dose required for treatment and therapeutic range for both drugs is approximately the same

172. Because of these similarities, Wyeth's formulators used Inderal LA as a model when they set out to develop Effexor XR. All that they had to do to develop Effexor XR was to substitute venlafaxine for propranolol in the Inderal formulation. In developing Effexor XR, the inventors used exactly the same

methods used to manufacture Inderal LA. They created venlafaxine spheroids using the same manufacturing methods used to create propranolol spheroids and then applied exactly the same solvent-based coating used to coat the propranolol spheroids. The availability of the Inderal LA formulation enabled the inventors to develop the Effexor XR formulation in only 6 months.

173. Notwithstanding the fact that the formulation of Effexor XR was identical to the formulation of Inderal, the Wyeth applicants failed to disclose to the PTO Inderal LA, its similarities to the Effexor XR formulation, or the use of the Inderal LA formulation to develop Effexor XR.

b. Wyeth's Failure to Disclose the Role of the Inderal LA Formulation Was Material.

174. During prosecution of Wyeth's patents, the examiner issued a rejection based on the patent that covers the Inderal LA product, U.S. Patent No. 4,138,475 to McAinsh (the "McAinsh patent").

175. Even after receiving express notice that the examiner viewed the propranolol formulation to be material, Wyeth chose not to disclose the Inderal LA product or its role in the development of Effexor XR to the patent examiner.

176. Rather than making such disclosures, Wyeth argued in the '328 patent application that propranolol was irrelevant because there is "a tremendous difference in the water solubilities" between propranolol and venlafaxine. This statement would have been of particular importance to the examiner because the

specification of the patents specifically states that extended release formulations of venlafaxine were "completely unexpected" because the hydrochloride of venlafaxine was extremely water soluble.

177. The label of Inderal LA directly contradicted Wyeth's arguments that propranolol and venlafaxine had significantly different solubilities. The label showed that, like venlafaxine, propranolol was readily soluble in water and had a peak blood level that occurred in about six hours.

178. The role of Inderal LA in the development of Effexor XR and the characteristics of propranolol were not disclosed in the McAinsh patent and would have been highly material to the patent examiner. Wyeth had a duty to disclose this information to the patent examiner who could not have been expected to have obtained the information himself, but properly relied upon Wyeth to comply with its duty of candor.

c. Wyeth Intentionally Failed to Disclose this Material Information About the Use of the Inderal LA Formulation to Develop Effexor XR.

179. In light of the examiner's rejection based on the McAinsh patent, the Wyeth applicants were aware of the significance of propranolol to the prosecution of patents related to Effexor XR.

180. Instead of disclosing the role of Inderal LA in the development of Effexor XR, however, Wyeth told the examiner that "the teaching of sustained

release formulation of microcrystalline cellulose and propranolol in McAinsh et al. is not deemed sufficiently relevant to venlafaxine because the two compounds are not structurally related."

181. This statement was a bald-faced lie. The inventors knew that the Inderal LA formulation was relevant to the patentability of Effexor XR. They used that very formulation to develop the extended release venlafaxine formulation that they sought to patent.

182. Rather than disclose Inderal LA during prosecution, Wyeth chose to disclose Lodine SR, another commercially available Wyeth product. In the background of invention section of the patent, the inventors disclosed that in developing extended release venlafaxine they started with the hydrogel formulation of Lodine SR. As the patent explains, however, numerous attempts to produce extended release venlafaxine tablets using hydrogel technology proved to be fruitless because "the compressed tablets were either physically unstable (poor compressibility or capping problems) or dissolved too rapidly."

183. The only inference that can be drawn from the inventors' choice to disclose their consideration of the Lodine SR formulation that did not work with venlafaxine but not their consideration of the Inderal LA formulation that did work is that they intended to deceive the patent examiner by making him believe that the Effexor XR formulation was new and novel.

D. Wyeth Engaged in Sham Litigation Against Seventeen Generic Manufacturers

184. Wyeth wrongfully listed all three of the fraudulently obtained method of use patents in the Orange Book.

185. At least 17 generic manufacturers sent Wyeth Paragraph IV certifications informing Wyeth they intended to manufacture AB-rated generic equivalents to Effexor XR and claiming their product would not infringe Wyeth's patents or that the patents were invalid and unenforceable. In each and every instance, Wyeth reflexively sued the generic for infringement of the '171, '958, and the '120 patents. Wyeth even sued a generic manufacturer (Osmotica) whose product was in a different form all together (tablet instead of capsule), not an AB-rated generic equivalent of Effexor XR, and could not possibly have infringed the '171, '958 and '120 patents, which covered only "encapsulated" extended release formulations of venlafaxine hydrochloride.

186. Wyeth knew that all three of the method of use patents were invalid and/or unenforceable. It knew that the clinical evidence did not support its comparative statements between Effexor XR and instant release Effexor. It knew that prior art existed for the claims it made in its formulation and method of use patents. Wyeth also knew that in the context of patent infringement litigation, where sophisticated parties acquire the true information about the circumstances of

the acquisition of a patent, it had no reasonable likelihood of succeeding on the merits of any of its infringement lawsuits.

187. Wyeth settled each and every infringement lawsuit (except the most recent) before a court issued a final decision as to whether the method of use patents were valid or enforceable.

1. Teva

188. On December 10, 2002, Teva filed an ANDA seeking approval of a generic version of Effexor XR. Teva's ANDA included Paragraph IV certifications that Wyeth's method of use patents were invalid, unenforceable, and would not be infringed by its generic extended release venlafaxine capsules.

189. As the first ANDA applicant to submit a Paragraph IV certification, Teva was entitled to be the only non-authorized generic on the market for 6 months. Typically, once a drug goes generic, the branded manufacturer sells both the branded version (at a high price) and an "authorized" generic version (at a much lower price), often selling the same exact pills in different bottles. During the first filer's exclusivity period, the branded manufacturer is the *only* firm able to market and sell a competing generic version of the drug because it is permitted to do so under the authority of its approved NDA rather than under an ANDA. Launching an authorized generic permits the branded company to capture some of the revenues and profits being earned in the generic market and, while it lowers the

price of the generics, it typically does not increase the rate at which pharmacies and patients substitute the generic for the brand.

190. On March 24, 2003, Wyeth brought suit against Teva in the District of New Jersey for infringement of the '171 patent, the '120 patent and the '958 patent. Wyeth charged Teva with infringement of claims 20-25 of the '171 patent, claims 1, 2, 13, and 14 of the '120 patent, and claims 1-6 of the '958 patent. All are method of use claims for either reducing the incidence of nausea or smoothing out the troughs and peaks in the blood serum. Wyeth did not assert that Teva infringed any of the formulation claims. Wyeth did not claim Teva infringed any other patents. The claim terms in dispute were: "extended release formulations," "spheroid," "with diminished incidence(s) of nausea and emesis," and "encapsulated."

191. Teva answered, denying the allegations and claiming that all the patents were invalid and not infringed. The case was closed per an order on January 20, 2006 after the parties filed under seal a Joint Settlement and Release Agreement on November 2, 2005.

192. As part of the settlement agreement, Wyeth gave Teva an "exclusive license" to sell a generic version of (immediate release) Effexor before the original compound patent for venlafaxine expired. The Husbands patent expired in June 2008; with Wyeth's permission, Teva obtained FDA approval and began selling

generic immediate release venlafaxine in August 2006 – over a year and a half before it otherwise could have.

193. Wyeth also agreed to refrain from selling an authorized generic version of immediate release Effexor until the Husbands patent expired, thereby giving Teva at least a year and a half as the *only* immediate release generic on the market.

194. Wyeth also gave Teva an "exclusive license" to sell a generic version of extended release Effexor XR beginning on July 1, 2010, with the possibility of an earlier launch if another generic entered or was successful in invalidating the method-of-use patents. This date was more than two years after the expiration of the Husbands patent. Except in certain limited circumstances (which did not come to pass), the period of exclusivity under the license expired eleven months later, on June 1, 2011. Thus, the agreement between Wyeth and Teva contemplated that Teva would have eleven months as the exclusive generic seller on the market rather than the six months provided by the Hatch-Waxman Act.

195. By entering into the settlement agreement, Teva agreed to delay the launch of generic Effexor XR until two years *after* the expiration of the only Wyeth patent capable of blocking generic competition to Effexor XR. Teva began selling generic extended release venlafaxine capsules on July 1, 2010 and was the only seller of generic Effexor XR until June 1, 2011.

196. Importantly from Teva's point of view, Wyeth agreed to refrain from selling an authorized generic version of Effexor XR during the term of Teva's license. By agreeing not to launch an authorized generic, Wyeth in effect agreed not to compete on price with Teva's generic product—*i.e.*, it agreed to sell Effexor XR only at the higher branded price and not at the lower generic price. This allowed Teva to maintain a relatively high generic price as the only generic manufacturer on the market and to earn higher profits than it otherwise would have earned, all at the expense of Plaintiffs and other generic purchasers.

197. The agreement between Wyeth and Teva was structured to encourage Wyeth to resolve all subsequent challenges to the '171, '120, and '958 patents prior to a court finding of invalidity, non-infringement, or unenforceability. Any such finding in a subsequent lawsuit against a potential manufacturer of generic Effexor XR would have triggered Teva's Hatch-Waxman exclusivity as the first paragraph IV filer. Consequently, upon information and belief, the license that Wyeth granted to Teva allowed Teva to enter the market earlier than June 2010 if any subsequent generic manufacturer succeeded in establishing invalidity, non-infringement, or unenforceability of Wyeth's three patents. Since such a result would have subjected Wyeth to generic competition from Teva earlier than July 2010, the agreement created an incentive in Wyeth to resolve subsequent generic cases without a court finding of invalidity, non-infringement, or unenforceability.

In fact, Wyeth resolved 15 of the next 16 cases prior to any such findings by a court. Teva launched its immediate release generic Effexor tablets in August 2006. By the end of 2007, approximately 96% of Wyeth's sales of immediate release Effexor tablets had converted to Teva's generic immediate release venlafaxine tablets. The availability of generic immediate release venlafaxine tablets from Teva did not significantly impact Wyeth's sales of Effexor XR.

198. On or about July 1, 2010, Teva launched its generic Effexor XR tablets. The launch of generic Effexor XR tablets caused Wyeth's sales of branded Effexor XR tablets to significantly decrease.

199. Had Wyeth not fraudulently obtained the '171, '120, and '958 patents, and/or not listed those patents in the Orange Book, and/or not brought a sham infringement lawsuit based on these patents, and/or not colluded with Teva to delay generic competition, Teva would have come to market with generic Effexor XR tablets in June 2008 and Wyeth would have launched an authorized generic at the same time.

2. Impax

200. On April 5, 2006, Wyeth brought suit against Impax Laboratories, Inc. ("Impax") in the District of Delaware for infringement of the '171 patent, the '120 patent and the '958 patent. Wyeth charged Impax with infringement of claims 20-

25 of the ‘171 patent, claims 1-6 of the ‘958 patent, and claims 1, 2, 13, and 14 of the ‘120 patent.

201. Impax answered, denying the allegations and claiming that all the patents were invalid, not infringed, and unenforceable.

202. On May 13, 2008, an order was entered at the joint request of the parties to have the court defer ruling on pending motions for summary judgment. The parties avoided a ruling on the merits. The case was closed per a consent judgment on July 15, 2008 after the parties filed under seal a Joint Settlement and Release Agreement on June 9, 2008. As part of the settlement, Wyeth agreed that Impax could enter the market with its generic version of Effexor XR on June 1, 2011, subject to earlier launch in limited circumstances, but in no event earlier than January 1, 2011.

3. Anchen

203. On April 12, 2006, Wyeth brought suit against Anchen Pharmaceuticals, Inc. (“Anchen”) in the Central District of California for infringement of the ‘171 patent, the ‘120 patent and the ‘958 patent. Wyeth charged Anchen with infringement of undefined claims. Anchen answered, denying the allegations, and claiming that all the patents were invalid and not infringed.

204. The case was closed per an order on November 3, 2008 after the parties filed under seal a Joint Settlement and Release Agreement on September 26, 2008.

205. As part of the settlement, Wyeth agreed that Anchen could enter the market with its generic version of Effexor XR on June 1, 2011, subject to earlier launch in limited circumstances, but in no event earlier than January 1, 2011.

4. Lupin

206. On March 12, 2007, Wyeth brought suit against Lupin Ltd. ("Lupin") in the District of Maryland for infringement of the '171 patent, the '120 patent and the '958 patent. Wyeth charged Lupin with infringement of claims 20-25 of the '171 patent, claims 1-6 of the '958 patent, and claims 1 and 2 of the '120 patent.

207. Lupin answered, denying the allegations and claiming that all the patents were invalid and not infringed.

208. The case was closed per an order on April 23, 2009, after the parties filed under seal a Joint Settlement and Release Motion on March 6, 2009.

209. As part of the settlement, Wyeth agreed that Lupin could enter the market with its generic version of Effexor XR on June 1, 2011, subject to earlier launch in limited circumstances, but in no event earlier than January 1, 2011.

5. Osmotica

210. On April 20, 2007, Wyeth brought suit against Osmotica Pharmaceuticals Corporation ("Osmotica") in the Eastern District of North Carolina for infringement of the '171 patent, the '120 patent, and the '958 patent. Wyeth charged Osmotica with infringement of the "asserted claims" which include claims 1-6 of the '958 patent and claim 1 of the '120 patent. The parties disputed the term "extended release formulations."

211. Osmotica sought to market a *tablet* form of extended release venlafaxine. Osmotica's NDA sought approval under the hybrid provisions of 505(b)(2) of the FDCA. Osmotica's product, by definition, was not an AB-rated generic equivalent of Effexor XR.

212. Osmotica answered, denying the allegations and claiming that all the patents were invalid, non-infringed, and were being misused to bar the introduction of venlafaxine tablets..

213. The case was closed per an order on March 19, 2008 after the parties filed under seal a Joint Settlement and Release Agreement on March 17, 2008.

214. As part of the settlement, Wyeth agreed to permit Osmotica to launch a non-AB rated extended release venlafaxine tablet pursuant to a royalty bearing license. Osmotica launched its extended release venlafaxine tablets in September 2008.

6. Sandoz

215. On June 22, 2007, Wyeth brought suit against Sandoz, Inc. ("Sandoz") in the Eastern District of North Carolina for infringement of the '171 patent, the '120 patent and the '958 patent. Wyeth charged Sandoz with direct infringement, active inducement of infringement, and contributory infringement of claims 20-25 of the '171 patent, claims 1-6 of the '958 patent, and claims 1, 2, 13, and 14 of the '120 patent.

216. Sandoz answered, denying the allegations and claiming that all the patents were invalid and not infringed.

217. The case was closed per an order on August 9, 2011 after the parties filed a stipulation of dismissal on August 8, 2011.

218. On information and belief, as part of the settlement, Wyeth agreed that Sandoz could enter the market with its generic version of Effexor XR.

7. Mylan

219. On July 6, 2007, Wyeth brought suit against Mylan Pharmaceuticals Inc. ("Mylan") in the Northern District of West Virginia for infringement of the '171 patent, the '120 patent and the '958 patent. Wyeth charged Mylan with direct infringement, active inducement of infringement, and contributory infringement of claims 20-25 of the '171 patent, claims 1-6 of the '958 patent, and claims 1, 2, 13, and 14 of the '120 patent.

220. Mylan answered, denying the allegations and claiming that all the patents were invalid and not infringed.

221. As part of its summary judgment briefing, Wyeth argued that any particular formulation of extended release venlafaxine hydrochloride was not novel – in direct contradiction to its representation in the method of use patent specifications that it was "completely unexpected that an extended release formulation … could be obtained."

222. On October 14, 2009 an order denied, in part, and granted, in part, Mylan's motions for summary judgment. Judge Keeley denied Mylan's motions regarding infringement and enablement, and granted Wyeth's motion regarding inventorship. Mylan's other defenses, including its invalidity defenses, remained unresolved.

223. The case was closed per a dismissal order on December 21, 2009 after the parties filed under seal a Joint Settlement and Release Motion on November 30, 2009.

224. As part of the settlement, Wyeth agreed that Mylan could enter the market with its generic version of Effexor XR on June 1, 2011, subject to earlier launch in limited circumstances, but in no event earlier than January 1, 2011.

8. Wockhardt

225. On August 8, 2007, Wyeth brought suit against Wockhardt USA LLC ("Wockhardt") in the Central District of California for infringement of the '171 patent, the '120 patent and the '958 patent.

226. Wockhardt answered, denying the allegations and claiming that all the patents were invalid, unenforceable, and not infringed.

227. On May 29, 2008, the district court denied Wyeth's motion to dismiss Wockhardt's inequitable conduct allegations. Trial was scheduled for September 14, 2010.

228. The case was closed per an order on May 19, 2009 after the parties filed under seal a Joint Settlement and Release Agreement.

229. As part of the settlement, Wyeth agreed that Wockhardt could enter the market with its generic version of Effexor XR on June 1, 2011, subject to earlier launch in limited circumstances, but in no event earlier than January 1, 2011.

230. Wockhardt launched its generic Effexor XR on or about June 1, 2011.

9. Biovail

231. On June 26, 2008, Wyeth brought suit against Biovail Corporation ("Biovail") in the District of Delaware for infringement of the '171 patent, the '120

patent and the ‘958 patent. Wyeth charged Biovail with infringement of undefined claims.

232. Biovail answered, denying the allegations, and claiming that all the patents were invalid and not infringed.

233. The case was closed per an order on March 19, 2010 after the parties filed under seal a Joint Motion to Enter Consent Judgment and to Enter Stipulated Order on November 12, 2009.

234. As part of the settlement, Wyeth agreed that Biovail could enter the market with its generic version of Effexor XR on June 1, 2011, subject to earlier launch in limited circumstances, but in no event earlier than January 1, 2011.

10. Apotex

235. On August 18, 2008, Wyeth brought suit against Apotex Inc. and Apotex Corp. (“Apotex”) in the Southern District of Florida for infringement of the ‘171 patent, the ‘120 patent and the ‘958 patent. Wyeth charged Apotex with infringement of claims 2-20 of the ‘171 patent, claims 1-6 of the ‘958 patent, and claims 1, 2, 13, and 14 of the ‘120 patent.

236. Apotex answered, denying the allegations, and claiming that all the patents were invalid, not infringed and unenforceable for inequitable conduct.

237. The case was closed per an order on September 15, 2010 after the parties filed under seal a Joint Settlement and Release Agreement dated August 11, 2010.

238. As part of the settlement, Wyeth agreed that Apotex could enter the market with its generic version of Effexor XR on June 1, 2011, subject to earlier launch in limited circumstances, but in no event earlier than January 1, 2011.

239. Apotex launched its generic version of Effexor XR on or about June 1, 2011.

11. Torrent

240. On January 8, 2009, Wyeth brought suit against Torrent Pharmaceuticals Limited and Torrent Pharma Inc. ("Torrent") in the District of Delaware for infringement of the '171 patent, the '120 patent and the '958 patent. Wyeth charged Torrent with infringement of claims undefined.

241. Torrent answered, denying the allegations and claiming that all the patents were invalid and not infringed.

242. The case was closed per an order on June 30, 2010 after the parties filed under seal a Joint Settlement and Release Agreement on May 6, 2010.

243. As part of the settlement, Wyeth agreed that Torrent could enter the market with its generic version of Effexor XR on June 1, 2011, subject to earlier launch in limited circumstances, but in no event earlier than January 1, 2011.

12. Cadila

244. On April 9, 2009, Wyeth brought suit against Cadila Healthcare Limited and Zydus Pharmaceuticals (USA) ("Cadila") in the District of Delaware for infringement of the '171 patent, the '120 patent and the '958 patent. Wyeth charged Cadila with infringement of claims undefined.

245. Cadila answered, denying the allegations, and claiming that all the patents were invalid, not infringed, and unenforceable.

246. The case was closed per an order on March 30, 2010 after the parties filed under seal a Joint Settlement and Release Agreement on January 28, 2010.

247. As part of the settlement, Wyeth agreed that Cadila could enter the market with its generic version of Effexor XR on June 1, 2011, subject to earlier launch in limited circumstances, but in no event earlier than January 1, 2011.

248. Cadila launched its generic version of Effexor XR in the Summer of 2011.

13. Orchid

249. On July 12, 2009, Wyeth brought suit against Orgenus Pharma Inc. and Orchid Chemicals and Pharmaceuticals (collectively, "Orchid") in the District of New Jersey for infringement of the '171 patent, the '120 patent and the '958 patent. Wyeth charged Orchid with infringement of claims undefined.

250. Orchid answered, denying the allegations, and claiming that all three patents were invalid, unenforceable, and not infringed.

251. A consent order of final judgment was entered on April 14, 2011.

252. As part of the settlement, Wyeth agreed that Orchid could enter the market with its generic version of Effexor XR on June 1, 2011, subject to earlier launch in limited circumstances, but in no event earlier than January 1, 2011.

14. Aurobindo

253. On April 22, 2010, Wyeth brought suit against Aurobindo Pharma Limited ("Aurobindo") in the District of New Jersey for the infringement of the '171 patent, the '120 patent and the '958 patent. Wyeth charged Aurobindo with infringement of claims undefined.

254. Aurobindo answered, denying the allegations, and claiming that all the patents were invalid and not infringed.

255. The case was closed per an order on February 10, 2011.

256. As part of the settlement, Wyeth agreed that Aurobindo could enter the market with its generic version of Effexor XR on June 1, 2011, subject to earlier launch in limited circumstances, but in no event earlier than January 1, 2011.

257. Aurobindo has introduced is generic version of Effexor XR.

15. Intellipharmaceutics

258. On July 1, 2010, Wyeth brought suit against Intellipharmaceutics International, Inc. ("IPI") in the Southern District of New York for infringement of the '171 patent, the '120 patent and the '958 patent.

259. IPI answered, denying the allegations and claiming that all three patents were invalid, unenforceable, and not infringed.

260. The case was closed by Order dated June 20, 2011 after the parties entered into a Stipulation of Dismissal.

261. Upon information and belief, as part of the settlement, Wyeth agreed that Intellipharmaceutics could enter the market with its generic version of Effexor XR.

16. Dr. Reddy's

262. On September 3, 2010, Wyeth brought suit against Dr. Reddy's Laboratories Ltd. ("Dr. Reddy's") in the District of New Jersey for infringement of the '171 patent, the '120 patent and the '958 patent.

263. Dr. Reddy's answered, denying the allegations and claiming that all three patents were invalid and not infringed.

264. The case was closed by an order dated April 28, 2011after the parties settledentered into a Stipulation and Order of dismissal on April 25, 2011.

265. As part of the settlement, Wyeth agreed that Dr. Reddy's could enter the market with its generic version of Effexor XR on June 1, 2011, subject to earlier launch in limited circumstances, but in no event earlier than January 1, 2011.

17. Nostrum

266. On April 12, 2011, Wyeth brought suit against Nostrum Pharmaceuticals LLC and Nostrum Laboratories, Inc. (collectively "Nostrum") for infringement of the '171 patent, the '120 patent and the '958 patent. As of this date, the case is still pending.

E. Prior Allegations and Evidence of the Invalidity and Unenforceability of Wyeth's Method of Use Patents

267. In patent infringement litigation against generic manufacturers, allegations about validity or enforceability, or rulings on the merits against a patent holder, are the kind of procedural developments that taint the patent with an issue regarding its validity or enforceability.

268. Here, Wyeth asserted that 17 different generic manufacturers infringed the method of use patents. Simply by filing suit, Wyeth kept each of the 17 generic equivalents of Effexor XR off the market for the shorter of two-and-a-half years or a decision on the merits. In answering Wyeth's claim of infringement, each of the generic companies claimed that the patents were invalid. Several of the generic companies also alleged the patents were unenforceable due

to inequitable conduct. The validity and enforceability was to be actively litigated between Wyeth and the generic manufacturers.

269. However, Wyeth settled each and every Effexor XR infringement suit before any court could render an opinion on the validity or enforceability of Wyeth's patents. Wyeth orchestrated settlements with the generics in order to bring an end to the litigation it started before a court could find the asserted method of use patents invalid or unenforceable. Such findings by a court would have triggered Teva's first-to-file exclusivity under the Hatch-Waxman Act and, by the terms of its settlement agreement with Wyeth, allowed Teva to enter the market with generic Effexor XR before the agreed-upon entry date of July 1, 2010.

270. Despite Wyeth's instituting 17 infringement lawsuits, and would-be generic competitors' allegations and evidence of invalidity and unenforceability, no court has, yet, entered an order determining the invalidity or enforceability of the '171, '958, and '120 patents.

271. Wyeth cannot insulate itself from liability for the anticompetitive effects of its fraudulent procurement of the method of use patents by bringing lawsuits that it knew that it would lose and settling with the alleged infringing generic companies before the merits could be adjudicated. If the terms are favorable, generic manufacturers have a significant incentive to accept Wyeth's

offer. But prescription drug purchasers are still harmed by Wyeth's anticompetitive scheme and sham litigation.

272. Settlement by the parties to the infringement actions cannot preclude those harmed by the anticompetitive effects of Wyeth's wrongful actions (in both obtaining the patents and filing infringement suits) from seeking recovery for their injuries.

VI. TRADE AND COMMERCE

273. The drugs at issue in this case are sold in interstate commerce, and the unlawful activities alleged herein have occurred in, and have had a substantial effect on, interstate commerce.

VII. MONOPOLY POWER AND MARKET DEFINITION

274. At all relevant times, Wyeth had monopoly power over Effexor XR and its generic equivalents because it had the power to maintain the price of the drug it sold as Effexor XR at supracompetitive levels without losing substantial sales to other products prescribed or used for the same purposes as Effexor XR, with the exception of generic extended-release venlafaxine hydrochloride capsules.

275. A small but significant, non-transitory price increase by Wyeth for Effexor XR would not have caused a significant loss of sales to other products prescribed and/or used for the same purposes as Effexor XR, with the exception of generic extended-release venlafaxine hydrochloride capsules.

276. Because of, among other reasons, psychotropic drugs' heterogeneous responses in different patient populations, Effexor XR is differentiated from all products other than AB-rated generic versions of Effexor XR.

277. Wyeth needed to control only Effexor XR and its AB-rated generic equivalents, and no other products, in order to maintain the price of Effexor XR profitably at supracompetitive prices without losing nearly all of its sales. Only the market entry of a competing, AB-rated generic version of Effexor XR would have made it impossible for Wyeth to maintain its current prices of Effexor XR without losing substantial sales.

278. Wyeth also sold Effexor XR at prices well in excess of marginal costs, and substantially in excess of the competitive price, and enjoyed high profit margins.

279. Wyeth has had, and exercised, the power to exclude competition to Effexor XR.

280. To the extent that Plaintiffs are legally required to prove monopoly power circumstantially by first defining a relevant product market, Plaintiffs allege that the relevant market is all extended release venlafaxine hydrochloride capsules – *i.e.*, Effexor XR (in all its forms and dosage strengths) and AB-rated bioequivalent extended release venlafaxine hydrochloride capsules. During the

period relevant to this case, Wyeth was able to profitably maintain the price of Effexor XR well above competitive levels.

281. Wyeth, at all relevant times, enjoyed high barriers to entry with respect to competition in the above defined relevant market due to patent and other regulatory protections, and high costs of entry and expansion.

282. The relevant geographic market is the United States and its territories.

283. Until July 2010, Wyeth's market share in the relevant market was 100%.

VIII. MARKET EFFECTS

284. Defendants' acts and practices had the purpose and effect of restraining competition unreasonably and injuring competition by protecting Effexor XR from generic competition. Defendants' actions allowed Wyeth to maintain a monopoly and exclude competition in the market for extended release venlafaxine hydrochloride capsules, *i.e.*, Effexor XR and its AB-rated generic equivalents, to the detriment of Plaintiffs and other purchasers of the drug.

285. Defendants' exclusionary conduct delayed generic competition and unlawfully enabled Wyeth to sell Effexor XR without generic competition. But for Defendants' illegal conduct, one or more generic competitors would have begun marketing AB-rated generic versions of Effexor XR much sooner than they actually were marketed, and, at all events, would have been on the market no later

than June 14, 2008. By way of examples and not limitation: (i) if there had been no fraud upon the PTO, the '171, '958, and '120 patents would not have issued, the patents would never have been listed in the Orange Book, and thus the patents would never have been the subject of infringement litigation that led to the 30-month Hatch-Waxman stay; (ii) if there had been no patents, there would have been no lawsuits, and, with no lawsuits, there would have been no settlements, all of which acted to further delay FDA approval and the timing of generic launch; (iii) if the lawsuits had not been brought, the 30-month Hatch-Waxman stay would never have been triggered, no settlements would have been necessary, and FDA approval would have been forthcoming by June of 2008 with generic makers ready, willing, and able to launch at that time.

286. The generic manufacturers seeking to sell generic Effexor XR had extensive experience in the pharmaceutical industry, including in obtaining approval for ANDAs and marketing generic pharmaceutical products.

287. Defendants' illegal acts to delay the introduction into the U.S. marketplace of any generic version of Effexor XR caused Plaintiffs to pay more than they would have paid for extended release venlafaxine hydrochloride capsules in the absence of that illegal conduct.

288. Typically, generic versions of brand-name drugs are initially priced significantly below the corresponding reference listed drug ("RLD") branded

counterpart to which they are AB-rated. As a result, upon generic entry, direct purchasers purchases of branded drugs are rapidly substituted for generic versions of the drug for some or all of their purchases. As more generic manufacturers enter the market, prices for generic versions of a drug predictably plunge even further because of competition among the generic manufacturers, and, correspondingly, the brand name drug continues to lose even more market share to the generics. This price competition enables all direct purchasers of the drugs to: (a) purchase generic versions of a drug at a substantially lower price, and/or (b) purchase the brand name drug at a reduced price. Consequently, brand name drug manufacturers have a keen financial interest in delaying the onset of generic competition, and purchasers experience substantial cost inflation from that delay.

289. If generic competitors had entered the market earlier and begun competing with Wyeth, Plaintiffs would have paid less for extended release venlafaxine hydrochloride capsules by (a) substituting purchases of less-expensive AB-rated generic Effexor XR for their purchases of more-expensive branded Effexor XR, (b) receiving discounts on their remaining branded Effexor XR purchases, and/or (c) purchasing generic Effexor XR at lower prices sooner. Likewise, if Wyeth had launched an authorized generic during the period of Teva's license, Plaintiffs would have paid a lower price for generic Effexor XR than they

actually paid during the time when Teva was the only generic manufacturer on the market.

290. Defendants' unlawful conduct deprived Plaintiffs of the benefits of competition that the antitrust laws were designed to ensure.

IX. ANTITRUST IMPACT

291. During the relevant period, Plaintiffs or their assignors purchased Effexor XR directly from Wyeth. As a result of Defendants' illegal conduct, Plaintiffs or their assignors were compelled to pay, and did pay, artificially inflated prices for their extended release venlafaxine hydrochloride requirements. Those prices were substantially greater than the prices that Plaintiffs (or their assignors) would have paid absent the illegal conduct alleged herein.

292. As a consequence, Plaintiffs have sustained substantial injuries to their business and property in the form of overcharges. The full amount and forms and components of such damages will be calculated after discovery and upon proof at trial.

X. CLAIMS FOR RELIEF

First Claim for Relief
Unlawful Monopolization (15 U.S.C. § 2)

293. Plaintiffs incorporate by reference the allegations in the above paragraphs. This claim is asserted against Defendant Wyeth.

294. As described above, from October 1997 until June 2010, Wyeth possessed monopoly power in the market for extended release venlafaxine hydrochloride capsules. No other manufacturer sold a competing version of extended release venlafaxine, whether branded or generic, before June 2010.

295. Wyeth willfully and unlawfully acquired and maintained its monopoly power in the extended release venlafaxine hydrochloride capsule market from June 2008 through June 2010 by engaging in an overarching anticompetitive scheme to keep generic equivalents from the market – not as a result of providing a superior product, business acumen, or historical accident.

296. Wyeth knowingly and intentionally engaged in an anticompetitive scheme designed to block and delay entry of AB-rated generic versions of Effexor XR to maintain their monopoly power. This scheme included:

a. obtaining the ‘171, ‘958, and ‘120 patents by misleading the PTO and failing to exercise the duty of good faith;

b. improperly listing the ‘171, ‘958, and ‘120 patents in the Orange Book;

c. engaging in sham litigation;

d. entering into an independently unlawful settlement agreement with Teva that further delayed generic entry; and

e. negotiating settlements with subsequent generic applicants to preserve and protect its monopoly and the market-division agreement negotiated with Teva.

297. By means of this scheme, Wyeth intentionally and wrongfully maintained its monopoly power with respect to Effexor XR in violation of Section 2 of the Sherman Act. As a result of this unlawful maintenance of monopoly power, Plaintiffs paid artificially inflated prices for their extended release venlafaxine hydrochloride requirements.

298. Plaintiffs have been injured in their business or property by Wyeth's antitrust violations. Their injury consists of having paid, and continuing to pay, higher prices for their extended release venlafaxine hydrochloride requirements than they would have paid in the absence of those violations. Such injury, consisting of "overcharges," is of the type that the antitrust laws were designed to prevent and flows from that which makes Wyeth's conduct unlawful.

299. Wyeth's anticompetitive conduct is not entitled to qualified *Noerr-Pennington* immunity.

300. Wyeth knowingly and intentionally engaged in sham litigation against manufacturers of AB-rated generic equivalents of Effexor XR. Wyeth repeatedly asserted that generic manufacturers' extended release venlafaxine formulations infringed its method of use patents, thereby automatically keeping each generic competitor off the market for at least 30 months. Wyeth intentionally and deceptively alleged that the generic manufacturers' products infringed its method of use patents. For each infringement suit, Wyeth knew at the time that it filed that

it had no realistic likelihood of success; that is, no realistic likelihood that a court would enforce the '171, '958, and '120 patents against a generic company. Wyeth knew, therefore, that no reasonable pharmaceutical manufacturer would have believed that it had a reasonable chance of succeeding on the merits of these infringement lawsuits. Wyeth filed these sham lawsuits for the purposes of using a governmental process (including the automatic 30 month stay of FDA approval) as an anticompetitive weapon to keep generics off the market.

301. Wyeth engaged in serial sham lawsuits as part of a pattern or practice of successive filing undertaken for the purposes of harassment, injuring market rivals, and unreasonably delaying generic entry. Wyeth filed 17 lawsuits, all asserting unenforceable patents, for the purpose of harassing generic manufacturers, keeping generics off the market, and preserving its Effexor XR monopoly. Wyeth settled each lawsuit before a court could find the patents unenforceable and negotiated deals with the generic companies that kept the first generic off the market until June 2010 and all other generics (including Wyeth's authorized generic) off the market until June 2011.

302. Wyeth engaged in four distinct *Walker Process* frauds.

303. First, Wyeth obtained method of use claims for extended release venlafaxine by fraudulently claiming clinical data showed Effexor XR reduced the incidence of nausea and vomiting associated with instant release Effexor. Wyeth

knew that its clinical data did not show a decreased incidence of nausea. Wyeth knew that this information would be material to the patent examiner. Wyeth intentionally withheld the truth about the clinical data in order to defraud the patent examiner into issuing patents that included method of use claims for the reduction in the incidence of vomiting.

304. Second, Wyeth obtained method of use claims for extended release venlafaxine by, first, failing to disclose its own Upton patent disclosed extended release venlafaxine and, later, failing to disclose that a patent examiner had found all method of use claims unpatentable in light of the Upton patent. Wyeth knew that both the Upton patent and the examiner's rejection of the method of use claims in light of the Upton patent would be material to the later patent examiner. Wyeth intentionally withheld the Upton patent and the related examiner's rejection in order to defraud the patent examiner into issuing patents that included method of use claims.

305. Third, Wyeth fraudulently claimed that an extended release version of Effexor was unexpected, despite knowing the Upton patent and the '589 PCT application previously disclosed extended release versions of Effexor. Wyeth intentionally failed to inform the examiner about the prior disclosures of extended release venlafaxine and further failed to correct its fraudulent representation that an

extended release version of venlafaxine was surprising in order to defraud the patent examiner into issuing patents that pertained to Effexor XR.

306. Fourth, Wyeth obtained the method of us claims for extended release venlafaxine by misrepresenting that it was "completely unexpected" that an extended release venlafaxine hydrochloride formulation could be obtained despite knowing and failing to disclose to the examiner that it developed the Effexor XR formulation by substituting venlafaxine for propranolol in the extended release formulation for its pre-existing Inderal LA product. Contrary to the representation to the PTO, Wyeth expected this formulation to work because venlafaxine and propranolol have similar solubilities in water and peak blood levels that occur in about six hours.

307. In addition to its fraudulent procurement and sham enforcement of the three method-of-use patents, Wyeth violated section 1 of the Sherman Act by entering into an independently unlawful settlement agreement with Teva in which, among other things, Teva agreed to delay its launch of its generic version of Effexor XR and Wyeth agreed to delay its launch of an authorized generic of the same drug.

308. This claim for relief accrued no earlier than June 2008.

Second Claim for Relief
Unlawful Conspiracy in Restraint of Trade (15 U.S.C. § 1)

309. Plaintiffs incorporate by reference the allegations in the above paragraphs. This claim is asserted against Defendants Wyeth and Teva.

310. In November 2005, Wyeth and Teva entered into a settlement agreement whereby, in return for various commercial benefits, Teva agreed to delay its launch of generic Effexor XR until July 1, 2010, subject to earlier launch upon the occurrence of specific events that did not happen, and Wyeth agreed to delay the launch of its authorized generic until the expiration of Teva's license, which occurred on June 1, 2011.

311. At all relevant times, Wyeth and Teva were potential competitors for sales of extended release venlafaxine and, but for their unlawful agreement, would have become actual competitors in June 2008. Likewise, Wyeth and Teva were at all relevant times potential competitors for sales of generic extended release venlafaxine and, but for their unlawful agreement, would have become actual competitors in June 2008. Their November 2005 settlement agreement amounted to a horizontal market-allocation agreement whereby Teva agreed not to compete with Effexor XR from the date of the settlement until July 2010 and Wyeth agreed not to compete with Teva from July 2010 until the expiration of Teva's license. Moreover, the agreement amounted to a horizontal price-fixing agreement whereby Wyeth agreed to sell Effexor XR only at the branded price and not at the generic

price from July 2010 until the expiration of Teva's license. These horizontal restraints are not in any way justified by Wyeth's non-existent intellectual property rights.

312. The November 2005 agreement constitutes a *per se* illegal horizontal conspiracy in restraint of trade. In the alternative, the agreement has had a substantially adverse effect on competition in the relevant market by: (a) allowing Wyeth to maintain its monopoly power and charge supracompetitive prices from June 2008 until July 2010—*i.e.*, for two years after the expiration of Wyeth's only valid and effective patent; and (b) by allowing Teva to maintain its position as the only generic seller on the market and to charge supracompetitive prices from July 2010 until June 1, 2011.

313. As a direct and proximate result of the unlawful November 2005 agreement, Teva delayed the launch of its generic Effexor XR product from June 2008 until July 2010, and Wyeth delayed the launch of its authorized generic from July 2010 until June 2011. Following execution of this agreement, Wyeth had an incentive to obtain, and did obtain, the agreement of all subsequent generic applicants to afford Teva eleven months of exclusivity rather than the six months it would have otherwise have enjoyed as the first ANDA filer pursuant to the Hatch-Waxman Act. But for the agreement, Teva would have launched generic Effexor XR in June 2008; Wyeth would have launched an authorized generic of Effexor

XR at the same time; and additional entrants would have launched their own generic products beginning on January 1, 2009.

314. As a direct and proximate result of the unlawful agreement, Plaintiffs have suffered injury to their business and property in the form of overcharges on Effexor XR and its generic equivalent. This injury is of the type the antitrust laws were designed to prevent and flows from that which makes Defendants' conduct unlawful.

315. This claim for relief accrued no earlier than June 2008.

XI. PRAYER FOR RELIEF

316. WHEREFORE, Plaintiffs respectfully pray for judgment against Defendants and for the following relief:

a. A determination by this Court that the acts alleged herein were and are unlawful under the antitrust laws of the United States;

b. With respect to the First Claim for Relief, a judgment against Wyeth for three times the damages actually sustained by Plaintiffs, as determined by a jury;

c. With respect to the Second Claim for Relief, a judgment against Wyeth and Teva for three times the damages actually sustained by Plaintiffs, as determined by a jury;

d. The costs of this suit, including a reasonable attorneys' fee; and

e. Such other and further relief as the Court deems just and proper.

XII. JURY DEMAND

317. Plaintiffs demand a trial by jury of all issues so triable.

Dated: December 23, 2011

Respectfully submitted,

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